

TITLE OF THE INVENTION

O-SUPERFAMILY CONOTOXIN PEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is related to U.S. provisional patent applications Serial No. 60/173,754 filed 30 December 1999, Serial No. 60/214,263 filed 26 June 2000, Serial No. 60/219,440 filed 20 July 2000 and Serial No. 60/243,412 filed 27 October 2000.

This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. The United States Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are referenced in the following text by author and date and are listed alphabetically by author in the appended bibliography.

Conus is a genus of predatory marine gastropods (snails) which envenomate their prey. Venomous cone snails use a highly developed apparatus to deliver their cocktail of toxic conotoxins into their prey. In fish-eating species such as *Conus magus* the cone detects the presence of the fish using chemosensors in its siphon. When close enough the cone extends its proboscis and impales the fish with a hollow harpoon-like tooth containing venom. This immobilizes the fish and enables the cone snail to wind it into its mouth via the tooth held at the end of its proboscis. For general information on *Conus* and their venom see the website address <http://grimwade.biochem.unimelb.edu.au/cone/reference.html>. Prey capture is accomplished through a sophisticated arsenal of peptides which target specific ion channel and receptor subtypes. Each *Conus* species venom appears to contain a unique set of 50-200 peptides. The composition of the venom differs greatly between species and between individual snails within each species, each optimally evolved to paralyse its prey. The active components of the venom are small peptides

toxins, typically 10-30 amino acid residues in length and are typically highly constrained peptides due to their high density of disulphide bonds.

The venoms consist of a large number of different peptide components that when separated exhibit a range of biological activities: when injected into mice they elicit a range of physiological responses from shaking to depression. The paralytic components of the venom that have been the focus of recent investigation are the α -, ω - and μ -conotoxins. All of these conotoxins act by preventing neuronal communication, but each targets a different aspect of the process to achieve this. The α -conotoxins target nicotinic ligand gated channels, the μ -conotoxins target the voltage-gated sodium channels and the ω -conotoxins target the voltage-gated calcium channels (Olivera et al., 1985; Olivera et al., 1990). For example a linkage has been established between α -, α A- & ψ -conotoxins and the nicotinic ligand-gated ion channel; ω -conotoxins and the voltage-gated calcium channel; μ -conotoxins and the voltage-gated sodium channel; δ -conotoxins and the voltage-gated sodium channel; κ -conotoxins and the voltage-gated potassium channel; conantokins and the ligand-gated glutamate (NMDA) channel. Five δ -conotoxins have been described: GmVIA (U.S. Patent No. 5,719,264); PVIA (U.S. Patent No. 5,739,276); TxVIA (Hillyard et al., 1989; Fainzilber et al., 1991); TxVIB (Fainzilber et al., 1991); NgVIA (Fainzilber et al., 1995); and TxIIA (Nakamura et al., 1996). For a partial list of *Conus* peptides and their amino acid sequences see the website address <http://pir.georgetown.edu>.

However, the structure and function of only a small minority of these peptides have been determined to date. For peptides where function has been determined, three classes of targets have been elucidated: voltage-gated ion channels; ligand-gated ion channels, and G-protein-linked receptors.

Conus peptides which target voltage-gated ion channels include those that delay the inactivation of sodium channels, as well as blockers specific for sodium channels, calcium channels and potassium channels. Peptides that target ligand-gated ion channels include antagonists of NMDA and serotonin receptors, as well as competitive and noncompetitive nicotinic receptor antagonists. Peptides which act on G-protein receptors include neurotensin and vasopressin receptor agonists. The unprecedented pharmaceutical selectivity of conotoxins is at least in part defined by a specific disulfide bond frameworks combined with hypervariable amino acids within disulfide loops (for a review see McIntosh et al., 1998).

Potassium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function.

These channels are vital in controlling the resting membrane potential in excitable cells and can be broadly sub-divided into three classes: voltage-gated K^+ channels, Ca^{2+} activated K^+ channels and ATP-sensitive K^+ channels. Many disorders are associated with abnormal flow of potassium ions through these channels. The identification of agents which would regulate the flow of potassium ions through each of these channel types would be useful in treating disorders associated with such abnormal flow.

It is desired to identify additional conotoxin peptides having activities of the above conopeptides, as well as conotoxin peptides having additional activities.

SUMMARY OF THE INVENTION

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds. The O-superfamily conotoxins include ω -conotoxins, κ -conotoxins, δ -conotoxins, μ O-conotoxins and GS conotoxin.

Thus, in one embodiment, the present invention is directed to the conotoxin peptides set forth in Table 2 and the corresponding peptides set forth in Table 1.

In a second embodiment, the present invention is directed to all of the propeptides and nucleic acid sequences encoding the propeptides or peptides set forth in Table 1.

In a third embodiment, the present invention is directed to derivatives or pharmaceutically acceptable salts of the conotoxin peptides disclosed herein. Examples of derivatives include peptides in which the Arg residues may be substituted by Lys, ornithine, homoargine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with ^{125}I -Tyr, meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Thr residues may be substituted with Ser or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; and the Asn, Ser, Thr or Hyp residues may be glycosylated. The halogen may be iodo, chloro, fluoro or bromo; preferably iodo for halogen substituted-Tyr and bromo for halogen-substituted Trp. The Tyr residues may also

be substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala. The aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including $n=8$. The Leu residues may be substituted with Leu (D). The Glu residues may be substituted with Glu. The Glu residues may be substituted with Glu. The Met residues may be substituted with norleucine (Nle). The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L).

Examples of synthetic aromatic amino acid include, but are not limited to, nitro-Phe, 4-substituted-Phe wherein the substituent is C_1-C_3 alkyl, carboxyl, hydroxymethyl, sulphomethyl, halo, phenyl, -CHO, -CN, -SO₃H and -NHAc. Examples of synthetic hydroxy containing amino acid, include, but are not limited to, such as 4-hydroxymethyl-Phe, 4-hydroxyphenyl-Gly, 2,6-dimethyl-Tyr and 5-amino-Tyr. Examples of synthetic basic amino acids include, but are not limited to, N-1-(2-pyrazolyl)-Arg, 2-(4-piperidinyl)-Gly, 2-(4-piperidinyl)-Ala, 2-[3-(2S)pyrrolidinyl]-Gly and 2-[3-(2S)pyrrolidinyl]-Ala. These and other synthetic basic amino acids, synthetic hydroxy containing amino acids or synthetic aromatic amino acids are described in Building Block Index, Version 3.0 (1999 Catalog, pages 4-47 for hydroxy containing amino acids and aromatic amino acids and pages 66-87 for basic amino acids; see also <http://www.amino-acids.com>), incorporated herein by reference, by and available from RSP Amino Acid Analogues, Inc., Worcester, MA. The residues containing protecting groups are deprotected using conventional techniques. Examples of synthetic acid amino acids include those derivatives bearing acidic functionality, including carboxyl, phosphate, sulfonate and synthetic tetrazolyl derivatives such as described by Ornstein et al. (1993) and in U.S. Patent No. 5,331,001, each incorporated herein by reference.

Optionally, in the peptides of the present invention, the Asn residues may be modified to contain an N-glycan and the Ser, Thr and Hyp residues may be modified to contain an O-glycan (e.g., g-N, g-S, g-T and g-Hyp). In accordance with the present invention, a glycan shall mean any N-, S- or O-linked mono-, di-, tri-, poly- or oligosaccharide that can be attached to any hydroxy, amino or thiol group of natural or modified amino acids by synthetic or enzymatic methodologies known in the art. The monosaccharides making up the glycan can include D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, D-galactosamine, D-glucosamine, D-N-acetyl-glucosamine (GlcNAc), D-N-acetyl-galactosamine (GalNAc), D-fucose or D-arabinose.

These saccharides may be structurally modified, e.g., with one or more O-sulfate, O-phosphate, O-acetyl or acidic groups, such as sialic acid, including combinations thereof. The glycan may also include similar polyhydroxy groups, such as D-penicillamine 2,5 and halogenated derivatives thereof or polypropylene glycol derivatives. The glycosidic linkage is beta and 1-4 or 1-3, preferably 1-3. The linkage between the glycan and the amino acid may be alpha or beta, preferably alpha and is 1-.

Core O-glycans have been described by Van de Steen et al. (1998), incorporated herein by reference. Mucin type O-linked oligosaccharides are attached to Ser or Thr (or other hydroxylated residues of the present peptides) by a GalNAc residue. The monosaccharide building blocks and the linkage attached to this first GalNAc residue define the "core glycans," of which eight have been identified. The type of glycosidic linkage (orientation and connectivities) are defined for each core glycan. Suitable glycans and glycan analogs are described further in U.S. Serial No. 09/420,797 filed 19 October 1999 and in PCT Application No. PCT/US99/24380 filed 19 October 1999 (PCT Published Application No. WO 00/23092), each incorporated herein by reference. A preferred glycan is Gal(β 1 \rightarrow 3)GalNAc(α 1 \rightarrow).

Optionally, in the peptides of general formula I and the specific peptides described herein, pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/(Glu or Asp) or Cys/Ala combinations. Sequential coupling by known methods (Barnay et al., 2000; Hruby et al., 1994; Bitan et al., 1997) allows replacement of native Cys bridges with lactam bridges. Thioether analogs may be readily synthesized using halo-Ala residues commercially available from RSP Amino Acid Analogues.

The present invention is further directed to derivatives of the above peptides and peptide derivatives which are acyclic permutations in which the cyclic permutants retain the native bridging pattern of native toxin. See, Craik et al. (2001).

In a fourth embodiment, the present invention is directed to uses of the conotoxin peptides described herein. In one aspect of this embodiment, members of the O-Superfamily conotoxins disclosed herein or a pharmaceutically acceptable salt or solvate thereof are used for regulating the flow of sodium ions through Na⁺ channels. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin

poisoning, Huntington's chorea, compression and entrapment neuropathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second aspect of this embodiment, a method of treating disorders associated with voltage gated ion channel disorders in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof. Thus, these peptides can be used to treat neurologic disorders, such as anticonvulsant agents, or as neuroprotective agents, such as for treating stroke, or as cardiovascular agents or for the management of pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome.

In a third aspect of this embodiment, a method of reducing/alleviating/decreasing the perception of pain by a subject or for inducing analgesia, particularly local analgesia, in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fourth aspect of this embodiment, a method for activating (i.e., opening) ATP-sensitive K^+ channels in a subject is provided which comprises administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth aspect of this embodiment, a method of treating disorders and conditions associated with proton-gated ion channels in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

Another embodiment of the invention contemplates a method of identifying compounds that mimic the therapeutic activity of the instant peptide, comprising the steps of: (a) conducting a biological assay on a test compound to determine the therapeutic activity; and (b) comparing the results obtained from the biological assay of the test compound to the results obtained from the

biological assay of the peptide. The peptide is labeled with any conventional label, preferably a radioiodine on an available Tyr. Thus, the invention is also directed to radioiodinated O-Superfamily conotoxins.

5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The invention relates to relatively short peptides (termed O-Superfamily conotoxins herein), about 20-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include three disulfide bonds.

10 The present invention, in another aspect, relates to a pharmaceutical composition comprising an effective amount of an O-Superfamily conotoxin peptide, a mutein thereof, an analog thereof, an active fragment thereof or pharmaceutically acceptable salts.

In one embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of delaying inactivation of sodium channels. The activity of δ -conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent No. 5,739,276, incorporated herein by reference. The treatment of disorders according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

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Sodium channels comprise a large and diverse group of proteins that, through maintenance of the cellular membrane potential, are fundamental in normal biological function. The therapeutic applications for compounds that regulate the flow of sodium ions through Na^+ channels are far-reaching and include treatments of a wide range of disease and injury states. Disorders which can be treated using these conopeptides include multiple sclerosis, other demyelinating diseases (such as acute disseminated encephalomyelitis, optic neuromyelitis, adrenoleukodystrophy, acute transverse myelitis, progressive multifocal leukoencephalopathy), sub-acute sclerosing panencephalomyelitis (SSPE), metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, spinal cord injury, botulinum toxin poisoning, Huntington's chorea, compression and entrapment neuropathies (such as carpal tunnel syndrome, ulnar nerve palsy), cardiovascular disorders (such as cardiac arrhythmias, congestive heart failure), reactive gliosis, hyperglycemia, immunosuppression, cocaine addiction, cancer, cognitive dysfunction, disorders resulting from

defects in neurotransmitter release (such as Eaton-Lambert syndrome), and reversal of the actions of curare and other neuromuscular blocking drugs.

In a second embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which has the capability of acting at voltage gated ion channels, particularly calcium channels, and are thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the partial or complete blockade of voltage gated ion channels of the central nervous system. The activity of ω -conotoxin peptides, members of the O-Superfamily, on calcium channels is described in U.S. Patent Nos. 5,587,454; 5,559,095 and 5,824,645, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

Voltage-gated calcium channels are present in neurons, and in cardiac, smooth, and skeletal muscle and other excitable cells, and are known to play a variety of roles in membrane excitability, muscle contraction, and cellular secretion, such as in synaptic transmission (McCleskey). In neuronal cells, voltage-gated calcium channels have been classified by their electrophysiological as well as by their biochemical (binding) properties. Six classes of physiologically distinct calcium channels have been identified to date, namely the T, L, N, P, Q, and R-type channels.

It is well known that an accumulation of calcium (calcium overload) in the brain is seen after anoxia, ischemia, migraine and other hyperactivity periods of the brain, such as after epileptic convulsions. An uncontrolled high concentration of calcium in the cells of the central nervous system (CNS) is known to cause most of the degenerative changes connected with the above diseases. Compounds which can block the calcium channels of brain cells are therefore useful in the treatment of stroke, anoxia, ischemia, migraine, psychosis, or epilepsy, any other convulsive disorder and in the prevention of the degenerative changes connected with the same.

Compounds blocking the so called L-type calcium channels in the CNS are useful for the treatment of the above disorders by directly blocking the calcium uptake in the CNS. Further, it is well known that the so called N- and P-types of calcium channels, as well as possibly other types of calcium channels, are involved in the regulation of neurotransmitter release. Compounds blocking the N- and/or P-types of calcium channels indirectly and very powerfully prevent calcium overload in the CNS after the hyperactivity periods of the brain as described above by inhibiting the enhanced neurotransmitter release seen after such hyperactivity periods of the CNS, and especially the

neurotoxic, enhanced glutamate release after such hyperactivity periods of the CNS. Furthermore, blockers of the N- and/or P-types of calcium channels, as dependent upon the selectivity of the compound in question, inhibit the release of various other neurotransmitters such as aspartate, GABA, glycine, dopamine, serotonin and noradrenaline.

Thus, the pharmaceutical compositions comprising a member of the O-Superfamily conotoxins of the present invention are useful as neuroprotectants, cardiovascular agents, anticonvulsants, analgesics or adjuvants to general anesthetics. A "neurological disorder or disease" is a disorder or disease of the nervous system including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage as in cardiac arrest or neonatal distress or epilepsy. In addition, a "neurological disorder or disease" is a disease state and condition in which a neuroprotectant, anticonvulsant, analgesic and/or as an adjunct in general anesthesia may be indicated, useful, recommended or prescribed.

More specifically, the present invention is directed to the use of a member of the O-Superfamily conotoxins for the treatment and alleviation of epilepsy and as a general anticonvulsant agent. The present invention is also directed to the use of these compounds for reducing neurotoxic injury associated with conditions of hypoxia, anoxia or ischemia which typically follows stroke, cerebrovascular accident, brain or spinal cord trauma, myocardial infarct, physical trauma, drowning, suffocation, perinatal asphyxia, or hypoglycemic events. The present invention is further directed to the use of O-superfamily-conotoxin peptides for treating pain, including acute and chronic pain, such as migraine, nociceptive and neuropathic pain. These peptides can further be used to treat spasticity, spinal cord injury or upper motor neuron syndrome. Other uses of these compounds are described in U.S. Patent No. 5,859,186, incorporated herein by reference.

A "neuroprotectant" is a compound capable of preventing the neuronal death associated with a neurological disorder or disease. An "anticonvulsant" is a compound capable of reducing convulsions produced by conditions such as simple partial seizures, complex partial seizures, status epilepticus, and trauma-induced seizures such as occur following head injury, including head surgery. An "analgesic" is a compound capable of relieving pain by altering perception of nociceptive stimuli without producing anesthesia or loss of consciousness. A "muscle relaxant" is a compound that reduces muscular tension. A "adjunct in general anesthesia" is a compound useful in conjunction with anesthetic agents in producing the loss of ability to perceive pain associated with the loss of consciousness.

The invention relates as well to methods useful for treatment of neurological disorders and diseases, including, but not limited to, global and focal ischemic and hemorrhagic stroke, head trauma, spinal cord injury, hypoxia-induced nerve cell damage such as in cardiac arrest or neonatal distress, epilepsy or other convulsive disorders without undesirable side effects.

Thus, in one aspect, the invention provides a method of reducing/alleviating/ decreasing the perception of pain by a subject or for inducing analgesia in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof. The pain may be acute, persistent, inflammatory or neuropathic pain.

In a second aspect, the invention provides a method of treating stroke, head or spinal cord trauma or injury, anoxia, hypoxia-induced nerve cell damage, ischemia, migraine, psychosis, anxiety, schizophrenia, inflammation, movement disorder, epilepsy, any other convulsive disorder or in the prevention of the degenerative changes connected with the same in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins of the present invention or a pharmaceutically acceptable salt or solvate thereof.

In a third embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins described herein which is useful as a local anesthetic for treating pain.

These conopeptides have long lasting anesthetic activity and are particularly useful for spinal anesthesia, either administered acutely for post-operative pain or via an intrathecal pump for severe chronic pain situations or for treatment of pain in epithelial tissue. The activity of μ O-conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. 09/590,386 (International Application No. PCT/US00/15779) filed on 9 June 2000, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

More specifically, in one aspect, the pain results from surgical or medical procedures, and a member of the O-Superfamily conotoxins as described herein is administered to the central nervous system (CNS), e.g. to the spine for spinal analgesia. In a second aspect, the pain is in an epithelial tissue region associated with damage or loss of epithelial tissue as a result of, for example, plastic surgery, canker sores, burns, sore throats, genital lesions, upper or lower gastrointestinal

bronchoscopy or endoscopy, intubation, dermatologic abrasions or chemical skin peels, and a member of the O-Superfamily conotoxins as described herein is administered to alleviate the associated pain.

In a fourth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of activating (i.e., opening) ATP-sensitive K^+ channels, and is thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the activation of ATP-sensitive K^+ channels. The activity of κ -conotoxin peptides, members of the O-Superfamily, on sodium channels is described in U.S. Patent Application No. _____ (International Application No. PCT/US00/25827) filed on 21 September 2000, incorporated herein by reference. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention. Thus the invention provides a method for treating cardiac ischemia, neuronal ischemia, ocular ischemia or asthma in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a member of the O-Superfamily conotoxins described herein or a pharmaceutically acceptable salt or solvate thereof.

In a fifth embodiment, such a pharmaceutical composition comprises a member of the O-Superfamily conotoxins which has the capability of acting on proton gated ion channels, and is thus useful for treating a disorder, disease or condition of a living animal body, including a human, which disorder, disease or condition is responsive to the partial or complete blockade of proton-gated ion channels. Since, these members of the O-Superfamily antagonize the proton-gated ion channel, they are useful as analgesics, especially for pain associated with inflammation, hematomas, cardiac or muscle ischemia, or cancer. Thus, in one aspect of the present invention, the peptides and derivatives disclosed herein are useful as analgesics, i.e., for the reduction in the perception of pain or the induction of analgesia. The treatment according to this embodiment comprises the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

The conotoxin peptides of the present invention are identified by isolation from *Conus* venom. Alternatively, the conotoxin peptides of the present invention are identified using recombinant DNA techniques by screening cDNA libraries of various *Conus* species using conventional techniques, such as the use of reverse-transcriptase polymerase chain reaction (RT-

PCR) or the use of degenerate probes. Primers for RT-PCR are based on conserved sequences in the signal sequence and 3' untranslated region of the conotoxin peptides genes isolated using degenerate probes. Clones which hybridize to degenerate probes are analyzed to identify those which meet minimal size requirements, i.e., clones having approximately 300 nucleotides (for a propeptide), as determined using PCR primers which flank the cDNA cloning sites for the specific cDNA library being examined. These minimal-sized clones and the clones produced by RT-PCR are then sequenced. The sequences are then examined for the presence of a peptide having the characteristics noted above for the O-Superfamily conotoxin peptides.

The conotoxin peptides described herein are sufficiently small to be chemically synthesized. General chemical syntheses for preparing the foregoing conotoxin peptides are described hereinafter. Various ones of the conotoxin peptides can also be obtained by isolation and purification from specific *Conus* species using the technique described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,514,774; 5,719,264; and 5,591,821, as well as in PCT published application WO 98/03189, the disclosures of which are incorporated herein by reference.

Although the conotoxin peptides of the present invention can be obtained by purification from cone snails, because the amounts of conotoxin peptides obtainable from individual snails are very small, the desired substantially pure conotoxin peptides are best practically obtained in commercially valuable amounts by chemical synthesis using solid-phase strategy. For example, the yield from a single cone snail may be about 10 micrograms or less of conotoxin peptide. By "substantially pure" is meant that the peptide is present in the substantial absence of other biological molecules of the same type; it is preferably present in an amount of at least about 85% purity and preferably at least about 95% purity. Chemical synthesis of biologically active conotoxin peptides depends of course upon correct determination of the amino acid sequence.

The conotoxin peptides can also be produced by recombinant DNA techniques well known in the art. Such techniques are described by Sambrook et al. (1989). A gene of interest (i.e., a gene that encodes a suitable conotoxin peptide) can be inserted into a cloning site of a suitable expression vector by using standard techniques. These techniques are well known to those skilled in the art. The expression vector containing the gene of interest may then be used to transfect the desired cell line. Standard transfection techniques such as calcium phosphate co-precipitation, DEAE-dextran transfection or electroporation may be utilized. A wide variety of host/expression vector combinations may be used to express a gene encoding a conotoxin peptide of interest. Such

combinations are well known to a skilled artisan. The peptides produced in this manner are isolated, reduced if necessary, and oxidized to form the correct disulfide bonds.

One method of forming disulfide bonds in the conotoxin peptides of the present invention is the air oxidation of the linear peptides for prolonged periods under cold room temperatures or at room temperature. This procedure results in the creation of a substantial amount of the bioactive, disulfide-linked peptides. The oxidized peptides are fractionated using reverse-phase high performance liquid chromatography (HPLC) or the like, to separate peptides having different linked configurations. Thereafter, either by comparing these fractions with the elution of the native material or by using a simple assay, the particular fraction having the correct linkage for maximum biological potency is easily determined. However, because of the dilution resulting from the presence of other fractions of less biopotency, a somewhat higher dosage may be required.

The peptides are synthesized by a suitable method, such as by exclusively solid-phase techniques, by partial solid-phase techniques, by fragment condensation or by classical solution couplings.

In conventional solution phase peptide synthesis, the peptide chain can be prepared by a series of coupling reactions in which constituent amino acids are added to the growing peptide chain in the desired sequence. Use of various coupling reagents, e.g., dicyclohexylcarbodiimide or diisopropylcarbonyldimidazole, various active esters, e.g., esters of N-hydroxyphthalimide or N-hydroxy-succinimide, and the various cleavage reagents, to carry out reaction in solution, with subsequent isolation and purification of intermediates, is well known classical peptide methodology. Classical solution synthesis is described in detail in the treatise, "Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden," (1974). Techniques of exclusively solid-phase synthesis are set forth in the textbook, "Solid-Phase Peptide Synthesis," (Stewart and Young, 1969), and are exemplified by the disclosure of U.S. Patent 4,105,603 (Vale et al., 1978). The fragment condensation method of synthesis is exemplified in U.S. Patent 3,972,859 (1976). Other available syntheses are exemplified by U.S. Patents No. 3,842,067 (1974) and 3,862,925 (1975). The synthesis of peptides containing γ -carboxyglutamic acid residues is exemplified by Rivier et al. (1987), Nishiuchi et al. (1993) and Zhou et al. (1996).

Common to such chemical syntheses is the protection of the labile side chain groups of the various amino acid moieties with suitable protecting groups which will prevent a chemical reaction from occurring at that site until the group is ultimately removed. Usually also common is the protection of an α -amino group on an amino acid or a fragment while that entity reacts at the

carboxyl group, followed by the selective removal of the α -amino protecting group to allow subsequent reaction to take place at that location. Accordingly, it is common that, as a step in such a synthesis, an intermediate compound is produced which includes each of the amino acid residues located in its desired sequence in the peptide chain with appropriate side-chain protecting groups linked to various ones of the residues having labile side chains.

As far as the selection of a side chain amino protecting group is concerned, generally one is chosen which is not removed during deprotection of the α -amino groups during the synthesis. However, for some amino acids, e.g., His, protection is not generally necessary. In selecting a particular side chain protecting group to be used in the synthesis of the peptides, the following general rules are followed: (a) the protecting group preferably retains its protecting properties and is not split off under coupling conditions, (b) the protecting group should be stable under the reaction conditions selected for removing the α -amino protecting group at each step of the synthesis, and (c) the side chain protecting group must be removable, upon the completion of the synthesis containing the desired amino acid sequence, under reaction conditions that will not undesirably alter the peptide chain.

It should be possible to prepare many, or even all, of these peptides using recombinant DNA technology. However, when peptides are not so prepared, they are preferably prepared using the Merrifield solid-phase synthesis, although other equivalent chemical syntheses known in the art can also be used as previously mentioned. Solid-phase synthesis is commenced from the C-terminus of the peptide by coupling a protected α -amino acid to a suitable resin. Such a starting material can be prepared by attaching an α -amino-protected amino acid by an ester linkage to a chloromethylated resin or a hydroxymethyl resin, or by an amide bond to a benzhydrylamine (BHA) resin or para-methylbenzhydrylamine (MBHA) resin. Preparation of the hydroxymethyl resin is described by Bodansky et al. (1966). Chloromethylated resins are commercially available from Bio Rad Laboratories (Richmond, CA) and from Lab. Systems, Inc. The preparation of such a resin is described by Stewart and Young (1969). BHA and MBHA resin supports are commercially available, and are generally used when the desired polypeptide being synthesized has an unsubstituted amide at the C-terminus. Thus, solid resin supports may be any of those known in the art, such as one having the formulae $-O-CH_2$ -resin support, $-NH$ BHA resin support, or $-NH$ -MBHA resin support. When the unsubstituted amide is desired, use of a BHA or MBHA resin is preferred, because cleavage directly gives the amide. In case the N-methyl amide is desired, it can be generated from an N-methyl BHA resin. Should other substituted amides be desired, the teaching

of U.S. Patent No. 4,569,967 (Kornreich et al., 1986) can be used, or should still other groups than the free acid be desired at the C-terminus, it may be preferable to synthesize the peptide using classical methods as set forth in the Houben-Weyl text (1974).

The C-terminal amino acid, protected by Boc or Fmoc and by a side-chain protecting group, if appropriate, can be first coupled to a chloromethylated resin according to the procedure set forth in K. Horiki et al. (1978), using KF in DMF at about 60°C for 24 hours with stirring, when a peptide having free acid at the C-terminus is to be synthesized. Following the coupling of the BOC-protected amino acid to the resin support, the α -amino protecting group is removed, as by using trifluoroacetic acid (TFA) in methylene chloride or TFA alone. The deprotection is carried out at a temperature between about 0°C and room temperature. Other standard cleaving reagents, such as HCl in dioxane, and conditions for removal of specific α -amino protecting groups may be used as described in Schroder & Lubke (1965).

After removal of the α -amino-protecting group, the remaining α -amino- and side chain-protected amino acids are coupled step-wise in the desired order to obtain the intermediate compound defined hereinbefore, or as an alternative to adding each amino acid separately in the synthesis, some of them may be coupled to one another prior to addition to the solid phase reactor. Selection of an appropriate coupling reagent is within the skill of the art. Particularly suitable as a coupling reagent is N,N'-dicyclohexylcarbodiimide (DCC, DIC, HBTU, HATU, TBTU in the presence of HOBt or HOAt).

The activating reagents used in the solid phase synthesis of the peptides are well known in the peptide art. Examples of suitable activating reagents are carbodiimides, such as N,N'-diisopropylcarbodiimide and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide. Other activating reagents and their use in peptide coupling are described by Schroder & Lubke (1965) and Kapoor (1970).

Each protected amino acid or amino acid sequence is introduced into the solid-phase reactor in about a twofold or more excess, and the coupling may be carried out in a medium of dimethylformamide (DMF):CH₂Cl₂ (1:1) or in DMF or CH₂Cl₂ alone. In cases where intermediate coupling occurs, the coupling procedure is repeated before removal of the α -amino protecting group prior to the coupling of the next amino acid. The success of the coupling reaction at each stage of the synthesis, if performed manually, is preferably monitored by the ninhydrin reaction, as described by Kaiser et al. (1970). Coupling reactions can be performed automatically, as on a Beckman 990 automatic synthesizer, using a program such as that reported in Rivier et al. (1978).

After the desired amino acid sequence has been completed, the intermediate peptide can be removed from the resin support by treatment with a reagent, such as liquid hydrogen fluoride or TFA (if using Fmoc chemistry), which not only cleaves the peptide from the resin but also cleaves all remaining side chain protecting groups and also the α -amino protecting group at the N-terminus if it was not previously removed to obtain the peptide in the form of the free acid. If Met is present in the sequence, the Boc protecting group is preferably first removed using trifluoroacetic acid (TFA)/ethanedithiol prior to cleaving the peptide from the resin with HF to eliminate potential S-alkylation. When using hydrogen fluoride or TFA for cleaving, one or more scavengers such as anisole, cresol, dimethyl sulfide and methylethyl sulfide are included in the reaction vessel.

Cyclization of the linear peptide is preferably affected, as opposed to cyclizing the peptide while a part of the peptido-resin, to create bonds between Cys residues. To effect such a disulfide cyclizing linkage, fully protected peptide can be cleaved from a hydroxymethylated resin or a chloromethylated resin support by ammonolysis, as is well known in the art, to yield the fully protected amide intermediate, which is thereafter suitably cyclized and deprotected. Alternatively, deprotection, as well as cleavage of the peptide from the above resins or a benzhydrylamine (BHA) resin or a methylbenzhydrylamine (MBHA), can take place at 0 °C with hydrofluoric acid (HF) or TFA, followed by oxidation as described above.

The peptides are also synthesized using an automatic synthesizer. Amino acids are sequentially coupled to an MBHA Rink resin (typically 100 mg of resin) beginning at the C-terminus using an Advanced Chemtech 357 Automatic Peptide Synthesizer. Couplings are carried out using 1,3-diisopropylcarbodiimide in N-methylpyrrolidinone (NMP) or by 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and diethylisopropylethylamine (DIEA). The Fmoc protecting group is removed by treatment with a 20% solution of piperidine in dimethylformamide (DMF). Resins are subsequently washed with DMF (twice), followed by methanol and NMP.

Mutens, analogs or active fragments, of the foregoing conotoxin peptides are also contemplated here. See, e.g., Hammerland et al, Eur. J. Pharmacol., 226, pp. 239-244 (1992). Derivative mutens, analogs or active fragments of the conotoxin peptides may be synthesized according to known techniques, including conservative amino acid substitutions, such as outlined in U.S. Pat. Nos. 5,545,723 (see particularly col. 2, line 50--col. 3, line 8); 5,534,615 (see particularly col. 19, line 45--col. 22, line 33); and 5,364,769 (see particularly col. 4, line 55--col. 7, line 26), each herein incorporated by reference.

Pharmaceutical compositions containing a compound of the present invention or its pharmaceutically acceptable salts or solvates as the active ingredient can be prepared according to conventional pharmaceutical compounding techniques. See, for example, *Remington's Pharmaceutical Sciences*, 18th Ed. (1990, Mack Publishing Co., Easton, PA). Typically, an antagonistic amount of the active ingredient will be admixed with a pharmaceutically acceptable carrier. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., intravenous, oral or parenteral. The compositions may further contain antioxidantizing agents, stabilizing agents, preservatives and the like. For examples of delivery methods see U.S. Patent No. 5,844,077, incorporated herein by reference.

"Pharmaceutical composition" means physically discrete coherent portions suitable for medical administration. "Pharmaceutical composition in dosage unit form" means physically discrete coherent units suitable for medical administration, each containing a daily dose or a multiple (up to four times) or a sub-multiple (down to a fortieth) of a daily dose of the active compound in association with a carrier and/or enclosed within an envelope. Whether the composition contains a daily dose, or for example, a half, a third or a quarter of a daily dose, will depend on whether the pharmaceutical composition is to be administered once or, for example, twice, three times or four times a day, respectively.

The term "salt", as used herein, denotes acidic and/or basic salts, formed with inorganic or organic acids and/or bases, preferably basic salts. While pharmaceutically acceptable salts are preferred, particularly when employing the compounds of the invention as medicaments, other salts find utility, for example, in processing these compounds, or where non-medicament-type uses are contemplated. Salts of these compounds may be prepared by art-recognized techniques.

Examples of such pharmaceutically acceptable salts include, but are not limited to, inorganic and organic addition salts, such as hydrochloride, sulphates, nitrates or phosphates and acetates, trifluoroacetates, propionates, succinates, benzoates, citrates, tartrates, fumarates, maleates, methane-sulfonates, isothionates, theophylline acetates, salicylates, respectively, or the like. Lower alkyl quaternary ammonium salts and the like are suitable, as well.

As used herein, the term "pharmaceutically acceptable" carrier means a non-toxic, inert solid, semi-solid liquid filler, diluent, encapsulating material, formulation auxiliary of any type, or simply a sterile aqueous medium, such as saline. Some examples of the materials that can serve as pharmaceutically acceptable carriers are sugars, such as lactose, glucose and sucrose, starches such as corn starch and potato starch, cellulose and its derivatives such as sodium carboxymethyl

cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt, gelatin, talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol, polyols such as glycerin, sorbitol, mannitol and polyethylene glycol; esters such as ethyl oleate and ethyl laurate, agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline, Ringer's solution; ethyl alcohol and phosphate buffer solutions, as well as other non-toxic compatible substances used in pharmaceutical formulations.

Wetting agents, emulsifiers and lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator. Examples of pharmaceutically acceptable antioxidants include, but are not limited to, water soluble antioxidants such as ascorbic acid, cysteine hydrochloride, sodium bisulfite, sodium metabisulfite, sodium sulfite, and the like; oil soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol and the like; and the metal chelating agents such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid and the like.

For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, lozenges, melts, powders, suspensions or emulsions. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, suspending agents, and the like in the case of oral liquid preparations (such as, for example, suspensions, elixirs and solutions); or carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like in the case of oral solid preparations (such as, for example, powders, capsules and tablets). Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar-coated or enteric-coated by standard techniques. The active agent can be encapsulated to make it stable to passage through the gastrointestinal tract while at the same time allowing for passage across the blood brain barrier. See for example, WO 96/11698.

For parenteral administration, the compound may be dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic

origin. The carrier may also contain other ingredients, for example, preservatives, suspending agents, solubilizing agents, buffers and the like. When the compounds are being administered intrathecally, they may also be dissolved in cerebrospinal fluid.

A variety of administration routes are available. The particular mode selected will depend of course, upon the particular drug selected, the severity of the disease state being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing clinically unacceptable adverse effects. Such modes of administration include oral, rectal, sublingual, topical, nasal, transdermal or parenteral routes. The term "parenteral" includes subcutaneous, intravenous, epidural, irrigation, intramuscular, release pumps, or infusion.

For example, administration of the active agent according to this invention may be achieved using any suitable delivery means, including:

- (a) pump (see, e.g., Luer & Hatton (1993), Zimm et al. (1984) and Ettinger et al. (1978));
- (b), microencapsulation (see, e.g., U.S. Patent Nos. 4,352,883; 4,353,888; and 5,084,350);
- (c) continuous release polymer implants (see, e.g., U.S. Patent No. 4,883,666);
- (d) macroencapsulation (see, e.g., U.S. Patent Nos. 5,284,761, 5,158,881, 4,976,859 and 4,968,733 and published PCT patent applications WO92/19195, WO 95/05452);
- (e) naked or unencapsulated cell grafts to the CNS (see, e.g., U.S. Patent Nos. 5,082,670 and 5,618,531);
- (f) injection, either subcutaneously, intravenously, intra-arterially, intramuscularly, or to other suitable site; or
- (g) oral administration, in capsule, liquid, tablet, pill, or prolonged release formulation.

In one embodiment of this invention, an active agent is delivered directly into the CNS, preferably to the brain ventricles, brain parenchyma, the intrathecal space or other suitable CNS location, most preferably intrathecally. This administration is preferably by a pump.

Alternatively, targeting therapies may be used to deliver the active agent more specifically to certain types of cell, by the use of targeting systems such as antibodies or cell specific ligands. Targeting may be desirable for a variety of reasons, e.g. if the agent is unacceptably toxic, or if it would otherwise require too high a dosage, or if it would not otherwise be able to enter the target cells.

The active agents, which are peptides, can also be administered in a cell based delivery system in which a DNA sequence encoding an active agent is introduced into cells designed for implantation in the body of the patient, especially in the spinal cord region. Suitable delivery systems are described in U.S. Patent No. 5,550,050 and published PCT Application Nos. WO 92/19195, WO 94/25503, WO 95/01203, WO 95/05452, WO 96/02286, WO 96/02646, WO 96/40871, WO 96/40959 and WO 97/12635. Suitable DNA sequences can be prepared synthetically for each active agent on the basis of the developed sequences and the known genetic code.

The active agent is preferably administered in a therapeutically effective amount. By a "therapeutically effective amount" or simply "effective amount" of an active compound is meant a sufficient amount of the compound to treat the desired condition at a reasonable benefit/risk ratio applicable to any medical treatment. The actual amount administered, and the rate and time-course of administration, will depend on the nature and severity of the condition being treated. Prescription of treatment, e.g. decisions on dosage, timing, etc., is within the responsibility of general practitioners or specialists, and typically takes account of the disorder to be treated, the condition of the individual patient, the site of delivery, the method of administration and other factors known to practitioners. Examples of techniques and protocols can be found in *Remington's Pharmaceutical Sciences*.

Dosage may be adjusted appropriately to achieve desired drug levels, locally or systemically. Typically the active agents of the present invention exhibit their effect at a dosage range from about 0.001 mg/kg to about 250 mg/kg, preferably from about 0.01 mg/kg to about 100 mg/kg of the active ingredient, more preferably from about 0.05 mg/kg to about 75 mg/kg. A suitable dose can be administered in multiple sub-doses per day. Typically, a dose or sub-dose may contain from about 0.1 mg to about 500 mg of the active ingredient per unit dosage form. A more preferred dosage will contain from about 0.5 mg to about 100 mg of active ingredient per unit dosage form. Dosages are generally initiated at lower levels and increased until desired effects are achieved. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Continuous dosing over, for example 24 hours or multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

For the treatment of pain, if the route of administration is directly to the CNS, the dosage contemplated is from about 1 ng to about 100 mg per day, preferably from about 100 ng to about 10 mg per day, more preferably from about 1 µg to about 100 µg per day. If administered

peripherally, the dosage contemplated is somewhat higher, from about 100 ng to about 1000 mg per day, preferably from about 10 µg to about 100 mg per day, more preferably from about 100 µg to about 10 mg per day. If the conopeptide is delivered by continuous infusion (e.g., by pump delivery, biodegradable polymer delivery or cell-based delivery), then a lower dosage is contemplated than for bolus delivery.

Advantageously, the compositions are formulated as dosage units, each unit being adapted to supply a fixed dose of active ingredients. Tablets, coated tablets, capsules, ampoules and suppositories are examples of dosage forms according to the invention.

It is only necessary that the active ingredient constitute an effective amount, i.e., such that a suitable effective dosage will be consistent with the dosage form employed in single or multiple unit doses. The exact individual dosages, as well as daily dosages, are determined according to standard medical principles under the direction of a physician or veterinarian for use humans or animals.

The pharmaceutical compositions will generally contain from about 0.0001 to 99 wt. %, preferably about 0.001 to 50 wt. %, more preferably about 0.01 to 10 wt.% of the active ingredient by weight of the total composition. In addition to the active agent, the pharmaceutical compositions and medicaments can also contain other pharmaceutically active compounds. Examples of other pharmaceutically active compounds include, but are not limited to, analgesic agents, cytokines and therapeutic agents in all of the major areas of clinical medicine. When used with other pharmaceutically active compounds, the conotoxin peptides of the present invention may be delivered in the form of drug cocktails. A cocktail is a mixture of any one of the compounds useful with this invention with another drug or agent. In this embodiment, a common administration vehicle (e.g., pill, tablet, implant, pump, injectable solution, etc.) would contain both the instant composition in combination supplementary potentiating agent. The individual drugs of the cocktail are each administered in therapeutically effective amounts. A therapeutically effective amount will be determined by the parameters described above; but, in any event, is that amount which establishes a level of the drugs in the area of body where the drugs are required for a period of time which is effective in attaining the desired effects.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art.

See, e.g., Maniatis *et al.*, 1982; Sambrook *et al.*, 1989; Ausubel *et al.*, 1992; Glover, 1985; Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988; Jakoby and Pastan, 1979; *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. 1984); *Transcription And Translation* (B. D. Hames & S. J. Higgins eds. 1984); *Culture Of Animal Cells* (R. I. Freshney, Alan R. Liss, Inc., 1987); *Immobilized Cells And Enzymes* (IRL Press, 1986); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); the treatise, *Methods In Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors For Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); *Methods In Enzymology*, Vols. 154 and 155 (Wu *et al.* eds.), *Immunochemical Methods In Cell And Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); *Handbook Of Experimental Immunology*, Volumes I-IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, *Essential Immunology*, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan *et al.*, *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986).

EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

EXAMPLE 1

Isolation of O-Superfamily Conotoxins

Crude venom was extracted from venom ducts (Cruz *et al.*, 1976), and the components were purified as previously described (Cartier *et al.*, 1996). The crude extract from venom ducts was purified by reverse phase liquid chromatography (RPLC) using a Vydac C₁₈ semi-preparative column (10 x 250 mm). Further purification of bioactive peaks was done on a Vydac C₁₈ analytical column (4.6 x 220 mm). The effluents were monitored at 220 nm. Peaks were collected, and aliquots were assayed for activity.

The amino acid sequence of the purified peptides were determined by standard methods. The purified peptides were reduced and alkylated prior to sequencing by automated Edman degradation on an Applied Biosystems 477A Protein Sequencer with a 120A Analyzer (DNA/Peptide Facility, University of Utah) (Martinez *et al.*, 1995; Shon *et al.*, 1994).

In accordance with this method, peptides δ -GmVIA, δ -PVIA, δ -SVIE, δ -SVIE [D1E], δ -NgVIA, δ -TxVIA and Israel TxVIA were obtained.

EXAMPLE 2

Synthesis of Conopeptides

The synthesis of conopeptides, either the mature toxins or the precursor peptides, was separately performed using conventional protection chemistry as described by Cartier et al. (1996). Briefly, the linear chains were built on Rink amide resin by Fmoc procedures with 2-(1H-benzotriol-1-yl)-1,1,3,3,-tetramethyluronium tetrafluoroborated coupling using an ABI model 430A peptide synthesizer with amino acid derivatives purchased from Bachem (Torrence CA). Orthogonal protection was used on cysteines: two cysteines were protected as the stable Cys(S-acetamidomethyl), while the other two cysteines were protected as the acid-labile Cys(S-trityl). After removal of the terminal Fmoc protecting group and cleavage of the peptides from the resins, the released peptides were precipitated by filtering the reaction mixture into -10°C methyl t-butyl ether, which removed the protecting groups except the Cys(S-acetamidomethyl). The peptides were dissolved in 0.1% TFA and 60% acetonitrile and purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted at a flow rate of 20 mL/min with a gradient of acetonitrile in 0.1% TFA.

The disulfide bridges in the three conopeptides were formed as described in Cartier et al. (1996). Briefly, the disulfide bridges between one pair of cysteines were formed by air oxidation which was judged to be complete by analytical RPLC. The monocyclic peptides were purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA. Removal of S-acetamidomethyl groups and closure of the disulfide bridge between the other pair of cysteines was carried out simultaneously by iodine oxidation. The cyclic peptides were purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA.

EXAMPLE 3

Isolation of DNA Encoding O-Superfamily Conotoxins

DNA coding for conotoxins described herein was isolated and cloned in accordance with conventional techniques using general procedures well known in the art, such as described in Olivera et al. (1996). Alternatively, cDNA libraries was prepared from *Conus* venom duct using

conventional techniques. DNA from single clones was amplified by conventional techniques using primers which correspond approximately to the M13 universal priming site and the M13 reverse universal priming site. Clones having a size of approximately 300-500 nucleotides were sequenced and screened for similarity in sequence to known O-Superfamily conotoxins, including the δ -conotoxins isolated in Example 1. The DNA sequences, encoded propeptide sequences and sequences of the mature toxins are set forth in the attached Table 1. DNA sequences coding for the mature toxin can also be prepared on the basis of the DNA sequences set forth on these pages. An alignment of the conotoxins is set forth in Table 2.

TABLE 1

**Sequences of Mature O-Superfamily Conotoxins,
Propeptides and DNA Encoding Propeptides**

Name: δ -GmVIA
Species: gloriamaris
Isolated: Yes
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCTGGACATTC
GTCACGGCTGATGACTCCGGAATGGAATGGAGATTCTTTTCCGAAGGCGGGTCA
CGAAATGGAGAACCCTCGAAGTCTCTAATCGGGTCAAGCCGTGCCGTAAAGAAGGTC
AACTTTGTGATCCGATATTTCAAACCTGCTGCCGTGGCTGGAATTGCGTTCTTTCTG
CGTCTGAAACTACCGTGATGTCTTCTCTCCCTC (SEQ ID NO:1)

Translation:

MKLT CMMIVAVLFLTAWTFVTADDSGNGMEILFPKAGHEMENLEVSNRVKPCRKEGQ
LCDPIFQNCCRGWNCVLFVCV (SEQ ID NO:2)

Toxin Sequence:

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-
Arg-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-^ (SEQ ID NO:3)

Name: δ -GmVIA [F15Y]
Species: gloriamaris

Toxin Sequence:

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Xaa5-Gln-Asn-Cys-Cys-
Arg-Gly-Xaa4-Asn-Cys-Val-Leu-Phe-Cys-Val-^ (SEQ ID NO:4)

Name: δ -GmVIA [F27Y]
Species: gloriamaris
Isolated: No

5 **Toxin Sequence:**

Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-Asn-Cys-Val-Leu-Xaa5-Cys-Val-[^] (SEQ ID NO:5)

10 **Name:** Omaria9
Species: omaria
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

GAAGCTGGTACGCCGTGCAGGTACCGGTCCGGAATCCCGGGTGCACATCATCATCA
TCGATCCATCTGTCCATCCATCCATTCATTTCGCTGCCAGACTATAATAAACATT
CAAGTCTCTCTTTCTTTTGTGTCTGACAGATCGATCAGGATGTGCCGTAGAGAAGC
TCAACTTTGTGATCCGATTTTTCAAAACGTGCTGCCATGGCTTGTTCGCTTTTGGTC
20 TGGCTCTAAAACCTACCGTGATGTCTTCTCTCCCTCTAGTAGTAGTAGGCGGCCGC
TCTAGAGGATCCAAGCTTACGTACGCGTGATGCGACGTCATAGCTCTTCTATAGTG
TCACCTAAATTCAATTCACCTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCT
GGCGTTACCCAACCTAATCGCCTTGACGACATCCCCCTTTCGCCAGCTGGCGTAAT
AGCGAAGAGCCCCGACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGA
25 ATGGGACGCGCCCTGTAGCGGCGCATTAT (SEQ ID NO:6)

Translation:

SIRMCRRQAQLCDPIFQNCCHGLFCVLVCV (SEQ ID NO:7)

30 **Toxin Sequence:**

Met-Cys-Arg-Arg-Xaa1-Ala-Gln-Leu-Cys-Asp-Xaa3-Ile-Phe-Gln-Asn-Cys-Cys-His-Gly-Leu-Phe-Cys-Val-Leu-Val-Cys-Val-[^] (SEQ ID NO:8)

35 **Name:** Tx6.11
Species: textile
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

GGCATTACCTAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT
GCTGTTCTTGACCGCCTGGACATTCGTCACGGCTGATGACTCCAGAAATGGAATGGA
GAATCTTTTTCCGAAGGCAGGTACGAAATGGAGAACCTCGAAGACTCTAAACACA
GGCACCAGGAGAGACCGGACACCGCGCACAAGAAGAGATGCTGCTACAGAGACA
45 GGTCAAGCCGTGTGCTAAAGAACATCA[^]CTTTGTGATCTGATTTTCAAAACGTCTG
CCGTGGCTGGTATTGCGTGTCTGTCTTGCACTGAAAGCTACCTGATGTGTTCTAC
TCCCATC (SEQ ID NO:9)

09749637 122800 082221 4E66460

Translation:

MKLT CMMIVAVLFLTAWTFVTADDSRNGMENLFPKAGHEMENLEDSKHRHQERPD TG
DKEEMLLQRQVKPCRKEHQLCDLIFQNCRCRGWYCVVLSCT (SEQ ID NO:10)

Toxin Sequence:

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-
Arg-Gly-Xaa4-Xaa5-Cys-Val-Val-Leu-Ser-Cys-Thr-^ (SEQ ID NO:11)

Name: Om6.6

Species: omaria

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCTGATGATCGTTGCCGTGCTGTCTTGACCGGCTGGACATTC
GTCACGGCTGATGACTCTGGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTCCACACGAGGG
CCCTTGTAATTGGCTTACACAAAATGCTGCAGTGTTATAATTGCATCATTTTTTTC
TGCCTATAAACTACCGTGATGTCTTCTCTCCCTC (SEQ ID NO:12)

Translation:

MKLTCLMIVAVLSLTGWTFVTADDSGNGLGNLFSNAHHEMKNPEASKLNKRCVPHEG
PCNWL TQNCSSGYNCIIFCL (SEQ ID NO:13)

Toxin Sequence:

Cys-Val-Xaa3-His-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Cys-Ser-Gly-Xaa5-
Asn-Cys-Ile-Ile-Phe-Phe-Cys-Leu-^ (SEQ ID NO:14)

Name: Da6.2

Species: dalli

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCTGCTGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGATGACTCCGGAATGGAATGGAGAATCTTTTTCCGAAGGCACGTCA
CGAAATGGAGAACCTCGAAGACTCTAAACACAGGCACAGGAGAGACCGGACACG
GGCGACAAAGAAGAGATGCTGTACAGAGACAGGTCAAGCCGTGTCGTAAGAAGAC
ATCAACTTTGTGATCTGATTTTTCAAACTGCTGCCGTGGCTGGTATTGCTTGCTTCG
TCCTTGATCTGAACTACCGTGATGTCTTCTCTCCATC (SEQ ID NO:15)

Translation:

MKLTCLLIIAVLFLTAWTFVTADDSGNGMENLFPKARHEMENLEDSKHRHQERPD TG
KEEMLLQRQVKPCRKEHQLCDLIFQNCRCRGWYCLLRPCI (SEQ ID NO:16)

Toxin Sequence:

Xaa2-Val-Lys-Xaa3-Cys-Arg-Lys-Xaa1-His-Gln-Leu-Cys-Asp-Leu-Ile-Phe-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-Xaa5-Cys-Leu-Leu-Arg-Xaa3-Cys-Ile-^ (SEQ ID NO:17)

Name: Da6.6

Species: dalli

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTATGCTGATCATTGCTGTGCTGTTCTTGACCGCTGGACATTC
GTCACGGCTGATGACTCCGGAAATGGAATGGAGAATCTTTTCCGAAGGCACGTCA
CGAAATGGAGAACCTCGAAGACTCTAAACACAGGCACCAGGAGAGACCGGACACG
GGCGACAAAGAAGAGATGCTGCTACAGAGACGGGTCAAGCCGTGCAGTGAAGAAG
GTCAACTTTGTGATCCACTTTCTCAAAACTGCTGCCGTGGCTGGCATTGCGTTCCTTG
CTCTTGCCTCTGAAACTACCGTGATGTCTTCTCTCCCATC (SEQ ID NO:18)

Translation:

MKLT CMLII AVLFLTA WFTV TADDSGNGMENLFPKARHEMENLED SKHRHQERPD TGD
KEEMLLQRRV KPCSEEGQLCDPLSQNCCRGWHCVLVSCV (SEQ ID NO:19)

Toxin Sequence:

Val-Lys-Xaa3-Cys-Ser-Xaa1-Xaa1-Gly-Gln-Leu-Cys-Asp-Xaa3-Leu-Ser-Gln-Asn-Cys-Cys-Arg-Gly-Xaa4-His-Cys-Val-Leu-Val-Ser-Cys-Val-^ (SEQ ID NO:20)

Name: δ-TxVIA

Species: textile

Isolated: Yes

Cloned: Yes

DNA Sequence:

AAACATCGCCAAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGAC
CGCCTGGACATTTGCCACGGCTGATGACCCGAGAAATGGATTGGGGAATCTTTTTC
GAATGCACATCACGAAATGAAGAACCCCGAAGCCTCTAAATGAACAAGAGGTGGT
GCAAACAAAGCGGTGAAATGTGTAATTTGTTAGACCAAAACTGCTGCGACGGCTAT
TGCATAGTACTTTGTCTGCACATAAACTGCCGTGATGTCTTCTCTCCCTCTGTGCT
ACCTGGCTTGATCTTTGATTGGCGCGTGTCTTCACTGGTTATGAACCCCCCCCCC
CCCCCCCCCCCCCTTCCGGCTCTCTGGAGGCCTCGGGGGTTCAACATCCAAATAA
AGTGACAG (SEQ ID NO:21)

Translation:

MKLT CMMIV AVLFLTA WTFATADDP RNCLGNLFSNAHHEMKNPEASKLNKRWCKQS
GEMCNLLDQNCDDGYCIVLVCT (SEQ ID NO:22)

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Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:23)

Name: δ-TxVIA [M8J]

Species: textile

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Xaa6-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:24)

Name: M6.4

Species: magus

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCTGGACATTTGCCACGGCTGATGACCCAGAAATGGATTGGGGAATCTTTTTCGAATGCACATCACGAAATGAAGAACCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAACAAAGCGGTGAAATGTGTGAATTTGTTAGACCAAAACTGCTGCGACGGCTATTGCATAGTACTGTCTGCACATAAACTGCCGTGATGTCTTCTCCTCCCTC (SEQ ID NO:25)

Translation:

MKLTCVMIVAVLFLTAWTFATADDPNGLGNLFSNAHHMKNPASKLNKRWCKQSGEMCNLLDQNCDDGYCIVLVCT (SEQ ID NO:26)

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:27)

Name: Israel TxIA

Species: textile

Isolated: Yes

Cloned: No

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-Xaa5-Cys-Ile-Val-Phe-Val-Cys-Thr-^ (SEQ ID NO:28)

Name: Di6.2

Species: distans

Isolated: No

09749637.12300

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT
GCCACGGCTGATGACCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAAACAAAGCG
GTGAAATGTGTAATTTGTTAGACCAAAACTGCTGCGACGGCTATTGCATAGTACTTG
TCTGCACATAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:29)

Translation:

MKLTCLMIVAVLFLTAWTFATADDPRLNGLNLFNSNAHHMKNPASKLNKRWCKQSG
EMCNLLDQNCDDGYCIVLVCT (SEQ ID NO:30)

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Asp-Gly-
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:31)

Name: Af6.9

Species: ammimalis

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT
GCCACGGCTGATGACCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGGTGCAAACAAAGCG
GTGAAATGTGTAATTTGTTAGACCAAAACTGCTGCGAGGGCTATTGCATAGTACTTG
TCTGCACATAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:32)

Translation:

MKLTCLMIVAVLFLTAWTFATADDPRLNGLNLFNSNAHHMKNPASKLNKRWCKQSG
EMCNLLDQNCCEGYCIVLVCT (SEQ ID NO:33)

Toxin Sequence:

Xaa4-Cys-Lys-Gln-Ser-Gly-Xaa1-Met-Cys-Asn-Leu-Leu-Asp-Gln-Asn-Cys-Cys-Xaa1-Gly-
Xaa5-Cys-Ile-Val-Leu-Val-Cys-Thr-^ (SEQ ID NO:34)

Name: Da6.4

Species: dalli

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTTTTGAAGGCACATCA

09749637.122800

CGAAATGAACCCCGAAGCCTCTAAGTTGAATGAGAGGTGCCTTGGTGGTGGTGAAG
TTTGTGATATCTTTTTCCACAATGCTGTGGCTATTGCATCTTCTTTCTGCACATAA
AACTACCGTGATGCTTCTCCTCCCTC (SEQ ID NO:35)

5 **Translation:**

MKLT CVMIVAVLFLTAWTFATADDPRNGLENLFLKAHHHEMNPEASKLNERCLGGGEV
CDIFPQCCGCGYILLFCT (SEQ ID NO:36)

Toxin Sequence:

- 10 Cys-Leu-Gly-Gly-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Gln-Cys-Cys-Gly-Xaa5-Cys-Ile-
Leu-Leu-Phe-Cys-Thr-^ (SEQ ID NO:37)

Name: Gm6.5
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

- 20 GCTTGCACGGTGAATTTGGCTTCACAGTTTCCACTGTCGCTTTTGGCATCATCTGAA
ACATCGCCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCG
CCTGGACATTTGCCACGGTGATGACCCAGAAATGGATTGGGGAATATTTTTTCGA
ATGCACATCACGAAATGAAGAATCCCGAAGCCTCTAAATTGAACAAGAGGTGCCGT
CTAGGGGCTGAAAGTTGTGATGTAATTTCACAAAAGTCTGCCAAGGCACGTGCGT
25 TTTTTCTGCTTACCATGATGTCTTCTATTCTCCTCTGTGCTACCTGGCTTGATCTTTC
ATTAGCGCGTGCCCTTCACTGGTTATGAACCCCTGATCCGACTCTCTGGCAGCCTC
GGGGGTTCAACATCCAAATAAACGACAGCACAATGACAAA (SEQ ID NO:38)

Translation:

- 30 MKLTCMMIVAVLFLTAWTFATADDPRNGLGNIFSNAHHEMNKNPEASKLNKRCRLGAE
SCDVISQNCQGTGVFFCLP (SEQ ID NO:39)

Toxin Sequence:

- 35 Cys-Arg-Leu-Gly-Ala-Xaa1-Ser-Cys-Asp-Val-Ile-Ser-Gln-Asn-Cys-Cys-Gln-Gly-Thr-Cys-Val-
Phe-Phe-Cys-Leu-Xaa3-^ (SEQ ID NO:40)

Name: Gm6.6
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

- 45 GGATCCTTGCACGGTGAATTTGGCTTCACAGTTTCCACTGTCGCTTTTCGCATCATC
CAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTG
ACCGCCTGGACATTCCGCCACGGCTGATGACCCAGAAATGGATTGGAGAACTTTT
TTCGAATACACATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGT

00021-299626

GCAACAAGCTGATGAATCTTGTAAATGTAATTTCACTTGACTGCTGCACCGGCTTAT
GCTTGGGATTCTGCGTATCGTGATGTCTTCTACTCCCCTCTGTgCTACCTGGCTTGAT
CTTTGATTGGCGTGTGCCTTTTCATTGGTTATGAACCCCTGATCCGATTCTTTGGCG
GCCTCGGGGGTTCAACATCCAATAAAGCGACAGCACAAATAAAAAA (SEQ ID
NO:41)

Translation:

MKLTCMMIVAVLFLTAWTFATADDPRNGLEKLFSENTHHEMKNPEASKLNKRCKQADE
SCNVFSLDCCTGLCLGFCVS (SEQ ID NO:42)

Toxin Sequence:

Cys-Lys-Gln-Ala-Asp-Xaa1-Ser-Cys-Asn-Val-Phe-Ser-Leu-Asp-Cys-Cys-Thr-Gly-Leu-Cys-
Leu-Gly-Phe-Cys-Val-Ser-^ (SEQ ID NO:43)

Name: Gm6.3
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC
GCCACGGCCATCACAGGAATGGATTGGGGAATCTTTTTCCGAAGAATCATCACGA
AATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTCATACGAGGGCC
CTTGTAATTGGCTTACACAAAACCTGCTGCGATGAGCTATGCGTATTTTCTGCCTAT
AAAACTAGCCTGATGT (SEQ ID NO:44)

Translation:

MKLTCMMIVAVLFLTTWTFATAITRNLGLNLFKNNHHEMKNPEASKLNKRCVPYEGPC
NWLTVQCCDELVCFFCL (SEQ ID NO:45)

Toxin Sequence:

Cys-Val-Xaa3-Xaa5-Xaa1-Gly-Xaa3-Cys-Asn-Xaa4-Leu-Thr-Gln-Asn-Cys-Cys-Asp-Xaa1-
Leu-Cys-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:46)

Name: M6.5
Species: magus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTCTTCTTGACCGTCTGGACATTC
GCCACGGCTGATGACTCCGGAATGGATTGGAGAACTTTTTCGAATGCACATCA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAAACAAGCTGAT
GAACCTTGTGATGTATTTTCACTTGAATGCTGCACCGGCATATGTCTTGGATTCTGC
ACGTGGTGATGTCTCCCTCCCCTC (SEQ ID NO:47)

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Translation:

MKLTCVMIVAVLFLTVWTFATADDSGNGLEKLFNSNAHHMKNPEASKLNKRCKQADE
PCDVFSLCCTGICLGFTW (SEQ ID NO:48)

Toxin Sequence:

Cys-Lys-Gln-Ala-Asp-Xaa1-Xaa3-Cys-Asp-Val-Phe-Ser-Leu-Xaa1-Cys-Cys-Thr-Gly-Ile-Cys-
Leu-Gly-Phe-Cys-Thr-Xaa4-^ (SEQ ID NO:49)

Name: Tx6.2
Species: textile
Isolated: No
Cloned: Yes

DNA Sequence:

GCCTTGCACGGTGAATTTGGCTTCATAGTTTCCACTGTCGTCTTTGGCATCATCCAA
AACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTCTGTCTTGACC
GCCTGGACATTCGCCACGGCTGATGACTCCAGCAATGGATTGGAGAATCTTTTTTG
AAGGCACATCACGAAATGAACCCCGAAGCCTCTAAGTTGAACGAGAGGTGCCTTGA
TGCTGGTGAAGTTTGTGATATTTTTTCCAACATGCTGCGGCTATTGCATTCTTCTT
TTCTGCGCATAAACTACCGTGATGTCTTCTACTCCCCTGTGCTACCTGGCTTGAT
CTTTGATTGGCGCGTACCCTTCACTGGTTATGAAACCCCTGATCCAGCTCTCTGGAG
GCCTCGGGGTTCAACATCCAAATAAAGCGACA (SEQ ID NO:50)

Translation:

MKLTCMMIVAVLFLTAWTFATADDSNGLENLFLKAHHMKNPEASKLNERCLDAGEV
CDIFPTCCGYCILLFCA (SEQ ID NO:51)

Toxin Sequence:

Cys-Ile-Asp-Ala-Gly-Xaa1-Val-Cys-Asp-Ile-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-Ile-
Leu-Leu-Phe-Cys-Ala-^ (SEQ ID NO:52)

Name: KK-1
Species: textile

Toxin Sequence:

Cys-Ile-Xaa1-Gln-Phe-Asp-Xaa3-Cys-Xaa1-Met-Ile-Arg-His-Thr-Cys-Cys-Val-Gly-Val-Cys-
Phe-Leu-Met-Ala-Cys-Ile-^ (SEQ ID NO:53)

Name: KK-2
Species: textile

Toxin Sequence:

Cys-Ala-Xaa3-Phe-Leu-His-Xaa3-Cys-Thr-Phe-Phe-Phe-Xaa3-Asn-Cys-Asn-Ser-Xaa5-

Cys-Val-Gln-Phe-Ile-Cys-Leu-[^] (SEQ ID NO:54)

Name: Om6.1
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
 GCCACGGCTGATGACCCAGAAATGGATTGGAGAATTTTTTCGAAGACACAACA
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCTAGCAGAACATG
 AAACCTGTAATATATTTACACAAAACCTGCTGCGAAGGCGTGTGCATTTTATCTGCG
 TACAAGTCCAGAGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:55)

Translation:

MKLTMMIVAVLFLTAWTFATADDPRNGLENFFSKTQHEMKNPESKLNKRCLAEHE
 TCNIFTQNCCEGVCIFICVQAPE (SEQ ID NO:56)

Toxin Sequence:

Cys-Leu-Ala-Xaa1-His-Xaa1-Thr-Cys-Asn-Ile-Phe-Thr-Gln-Asn-Cys-Cys-Xaa1-Gly-Val-Cys-
 Ile-Phe-Ile-Cys-Val-Gln-Ala-Xaa3-Xaa1-[^] (SEQ ID NO:57)

Name: Om6.3
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACTGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTG
 GCCACGGCTGAAGACCCAGACATGGATTGGAGAATCTTTTTCGAAGGCACATCA
 CGAAATGAAGAACCCTGAAGACTCTAAATTGGACAAGAGGTGCATTCCACATTTTG
 ACCCTTGTGACCCGATACGCCACACCTGCTGCTTTGGCCTGTGCCTACTAATAGCCT
 GCATCTAAAACCTGCCGTGATGTCTTCTCTCCCATC (SEQ ID NO:58)

Translation:

MKLTVMIVAVLFLTAWTFATAEDPRHGLNLFSAHHEMKNPEDSKLDRICIPHFDP
 CDPIRHTCCFGLCLLIACI (SEQ ID NO:59)

Toxin Sequence:

Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-
 Leu-Leu-Ile-Ala-Cys-Ile-[^] (SEQ ID NO:60)

Name: Om6.4
Species: omaria

00827.266426

DNA Sequence:
ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT

GCCACGGCTGATGACCCCGAGAAATGGATTGGATAATCGTTTTTCGAAGGCACGTCA
CGAAATGAATAACCGCAGAGCCTCTAAATTGAACAAGAGGTGCCTTGAGTTTGGTG
AACTTTGTAATTTTTTTTCCCAACCTGCTGCGGCTATTGCGTTCTTCTGTCTGCCTA
TAAACTACCGTGATGTCTTCTCTCCCTC (SEQ ID NO:67)

Translation:

MKLTCVMIVAVLFLTAWTFATADDPRNGLDNRFASKARHEMNRRASKLNKRCLEFGE
LCNFFFTCCGYCVLLVCL (SEQ ID NO:68)

Toxin Sequence:

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Leu-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-
Val-Leu-Leu-Val-Cys-Leu-^ (SEQ ID NO:69)

Name: Da6.5

Species: dalli

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT
GTCATGGCTGATGACTCCGGAATGGATTGGAAAATCTGTTTTCGAAGGCACATCA
CGAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGGTGCGCTCAAAGCAGTG
AATTATGTGATGCGCTGGACTCAGACTGCTGCAGTGGTGTTTGCATGGTATTTTTCT
GCCTATAAACTGCCGTGATGTCTTCTATCCCTC (SEQ ID NO:70)

Translation:

MKLTCVMIVAVLFLTAWTFVMADDSGNLENLFSKAHHHEMKNPEASKLNKRC AQSS
LCDALDSDCCSGVCMVFFCL (SEQ ID NO:71)

Toxin Sequence:

Cys-Ala-Gln-Ser-Ser-Xaa1-Leu-Cys-Asp-Ala-Leu-Asp-Ser-Asp-Cys-Cys-Ser-Gly-Val-Cys-
Met-Val-Phe-Phe-Cys-Leu-^ (SEQ ID NO:72)

Name: Di6.4

Species: distans

Isolated: No

Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGAAGACCCCGAGATGGATTGAGGAATCTTTATCGAATGCACGTCA
TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACGAGAGGTGCCTTGGGTTTGGTG
AAGCTTGCTTTATGCTTTATTACAGACTGTCAGCTATTGCGTTGGTGCTGTCTGCCT
ATAAACTACCGTGATGTCTTCTACTCCCATC (SEQ ID NO:73)

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Translation:

MKLTTCVMTVAVLFLTAWTFVTAEDPRDGLRNLLSNARHEMKNPEASKLNERCLGFGE
ACLMLYSDCCSYCVGAVCL (SEQ ID NO:74)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Cys-Ser-Xaa5-Cys-Val-
Gly-Ala-Val-Cys-Leu-^ (SEQ ID NO:75)

10 **Name:** Pn6.2
Species: pennaceus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCCTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT
GCCACGGCTGAAGACCCAGAAATGGATTGGAGAATCTTTTTTCGAAGGCACATCA
CGAAATGAAGAACCCTGAAGACTCTAAATTGGACAAGAGGTGCGTTAAATATCTTG
ACCTTTGTGACATGTTACGCCACACCTGCTGCTTTGGCCTGTGCGTACTAATAGCCT
GCATCTAAAACTGCCGTGATGTCTTCTACTCCCATC (SEQ ID NO:76)

Translation:

25 MKLTCLMTVAVLFLTAWTFATAEDPRNGLENLFSKAHHHEMKNPEDSKLDKRCVKYLD
PCDMLRHTCCFGLCVLIACI (SEQ ID NO:77)

Toxin Sequence:

30 Cys-Val-Lys-Xaa5-Leu-Asp-Xaa3-Cys-Asp-Met-Leu-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-
Val-Leu-Ile-Ala-Cys-Ile-^ (SEQ ID NO:78)

35 **Name:** Pn6.3
Species: pennaceus
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTT
GCCACGGCTGATGACCCAGAAATGGATTGGGGAATCTTTTTTCGAATGCACATCAC
GAAATGAAGAACCCCGAAGCTTCTAAATTGAACGAGAGGTGCGTTGGGTTTGGTGA
AGTTTGCAATTTCTTTTTTCCAACTGCTGCAGCTATTGCGTGTGCTTGTGCTGCCTA
45 TAAAACTACCGTGATGTCTTCTATTCCCTC (SEQ ID NO:79)

Translation:

09749637.122800

MKLT CVMIVAVLFLTAWTFATADDPRNGLGNLFSNAHHMKNP EASKLNERCLGFGE
VCNFFFPNCCSYCVALVCL (SEQ ID NO:80)

5 **Toxin Sequence:**

Cys-Leu-Gly-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Xaa5-Cys-Val-
Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:81)

10

Name: Pn6.4
Species: pennaceus
Isolated: No
Cloned: Yes

15

DNA Sequence:

ATGAAACTGACGTGCGTGATGCTCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GCCACGGCTGATGACTCCAGCAATGGACTGGAGAATCTTTTTCGAAGGCACATCA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCATTCCACAATTTG
ATCCTTGTGACATGGTACGTACACTTGCTGCAAAGGGTGTGCGTACTAATAGCCT
GCTCTAAAACTGCGTGATGTCTTCATCTCCCTC (SEQ ID NO:82)

20

Translation:

MKLT CVMIVAVLFLTAWTFATADDSSNGLENLFSKAHHMKNP EASKLNKRCIPQFDP
CDMVRHTCCKGLCVLIACSKTA (SEQ ID NO:83)

25

Toxin Sequence:

Cys-Ile-Xaa3-Gln-Phe-Asp-Xaa3-Cys-Asp-Met-Val-Arg-His-Thr-Cys-Cys-Lys-Gly-Leu-Cys-
Val-Leu-Ile-Ala-Cys-Ser-Lys-Thr-Ala-^ (SEQ ID NO:84)

30

35

Name: Pn6.7
Species: pennaceus
Isolated: No
Cloned: Yes

40

DNA Sequence:

ATGAAACTGACGTGCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GCCACGGCTGATGACCCAGAAATGGATTGGAGAATTTTTTTTCGAAGACACAACA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCAAAGCAGAAAAGT
GAAGCTTGTAATATAATTACACAAAACCTGCTGCGACGGCAAGTGCCTTTTTTCTG
ATACAAATCCAGAGTGATGTCTTCTCTCCCATC (SEQ ID NO:85)

45

008221-7E964760

Translation:

MKLTCLMIVAVLFLTAWTFATADDPNGLNFFSKTQHEMKNPEASKLNKRCKAESEA
CNIITQNCCDGGKCLFFCIPIE (SEQ ID NO:86)

Toxin Sequence:

Cys-Lys-Ala-Xaa1-Ser-Xaa1-Ala-Cys-Asn-Ile-Ile-Thr-Gln-Asn-Cys-Cys-Asp-Gly-Lys-Cys-
Leu-Phe-Phe-Cys-Ile-Gln-Ile-Xaa3-Xaa1-[^] (SEQ ID NO:87)

Name: Omaria3
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCATCATCGATCCATCTGTCCATCCATCCATTCAATTCGCT
GCCAGACTGTCATAAATATTCGAGTCTCTCCTTCTGTTGTATCTGACAGATTGAAC
AAGAGGTGCATTGACGGTGGTGAAATTTGTGATATTTTTTCCAACTGCTGCAGT
GGGTGGTGCAATTATTCTCGTCTGCGCATGAAACTACCGTGATGTCTTCTACTCCCTC
TAGTAGTAGTAGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGA
CGTCATAGCTCTTCTATAGTGTACCTAAATTCAATCACTGGCCGTCGTTTACAAC
GTCTGTGACTGGGAAAACCTGGCGTTACCCAACCTTAATCGCCTTGCAGCACATCCCC
CTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCAACAGT
TTGCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGGGC
GGGTGTGGTGGGTaCGCGCAGCGTGACCGGTACACTTGCCAGCGCCCTAGCGCCCGC
TCCTTTTGCTTTCTTCCCTTCCTTCTCGCCACCGTTcGCCCCGGGTTTTCCCGTCaAG
CTC (SEQ ID NO:88)

Translation:

LNKRCIDGGEICDIFFPNCCSGWCILVCA (SEQ ID NO:89)

Toxin Sequence:

Cys-Ile-Asp-Gly-Gly-Xaa1-Ile-Cys-Asp-Ile-Phe-Phe-Xaa3-Asn-Cys-Cys-Ser-Gly-Xaa4-Cys-
Ile-Ile-Leu-Val-Cys-Ala-[^] (SEQ ID NO:90)

Name: Omaria1
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTCAATTCGCTGCC
 AGACTGTCATAAAATATTCGAGTCTCTCTTGTGTTGATCTGACAGATTGAACAAG
 AGGTGCCTTGACGGTGGTGAAATTTGTGGTATTTTGTTCCTCAAGCTGCTGCAGTGCG
 5 TGGTGCATTGTTCTCGTCTGCGCATGAACTACCGTGATGTCTTCTACTCCCTCTAG
 TAGTAGTAGGCGGCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGT
 CATAGCTCTTCTATAGTGTACCTAAATTCATTCACCTGGCCGTCGTTTACAACGTC
 GTGACTGGGAAAACCTGGCGTTACCCAACCTTAATCGCCTTGACGACATCCCCCTT
 TCGCCAGCTGGCGTAATAGCGAAGAGGCCGACCGATCGCCCTTCCCAACAAGTT
 10 GCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGGGCGG
 GTGTGGTGGTTACGCGCACCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCT
 CCTTTCGCTTCTCTCCCTTCTTCTCGCACGTTTCGGCCGGCTTCCCCGTCAAGCTCT
 AATCGGGGGCTTCCCTTTTA (SEQ ID NO:91)

Translation:

LNKRCLDGGEICILFPSCSGWCIVLVCA (SEQ ID NO:92)

Toxin Sequence:

Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Val-Leu-Val-Cys-Ala-[^] (SEQ ID NO:93)

Name: Marm7
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCATCGATCCATCTGTCCATCCATCCATCCATTCAATTCGCTGCC
 AGACTGTAATAAAATATTCGAGTCTCTCTTCTGTTTGTATCTGACAGATTGAACAAG
 AGGTGCCTTGAGTTTGGTGAAAGTTTGTAATTTTTTTTCCCAACCTGCTGCGGCTATT
 35 GCGTCTCTTCTGTCTGCTATAAACTACCGTGATGTCTTCTACTCCCTCTAGTAGT
 AGTAGGCGGCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATA
 GCTCTTCTATAGTGTACCTAAATTCATTCACCTGGCCGTCGTTTACAACGTCGTGA
 CTGGGAAAACCTGGCGTTACCCAACCTAATCGCCTTGCAGCAGATCCCCCTTTCGC
 CAGCTGGCGTAATAGCGAAGAGGCCGCGACCGATCGCCCTTCCCAACAGTTGCGCA
 40 GCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAAGCGGGCGGGTGTG
 GTGTGTACGCGCAGCGTGACCGCTACACTTGACGCGCCCTAGCGCCCGCTCCTTTCG
 CTTTCTCCCTTCTTCTCGCCACGTTTCGGCGGCTTCCCCGTCAA (SEQ ID NO:94)

Translation:

LNKRCLFGEVCNFFFTCCGYCVLLVCL (SEQ ID NO:95)

09749637.1.22800

Toxin Sequence:

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-Val-Leu-Leu-Val-Cys-Leu-[^] (SEQ ID NO:96)

Name: Marm12
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GAAAGCTGGTACGCCTGCAGGTACCGGTCCGGAATTCCTGGGTCGACATCATCATC
 ATATTCGGATCCATCTGTCCATCCATCCATTCAATTCATTCGTCAGACTGTAATAA
 ATATTCGAGTTTCTCCTTCTGTTGTATCTGACAGGTTGAACAAGAGGTGCCAAGAG
 TTCGGTGAAGTTTGTAATTTTTTTTCCAGACTGCTCGCGCTATTGCGTCTCTTTAC
 TCTGCATATAAACTACCGTGATGTCTTCTCTTCCCATCTAGTAGTAGTAGTAGTAG
 TAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGC
 TCTTCTATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTACAACCGTCGTGAC
 TGGGAAAACCTGGCGTTCCCAACTTAATTCGCCTTGCAGCACAT (SEQ ID NO:97)

Translation:

LNKRCQEFGEVCNFFFPDCCGYCVLLLCI (SEQ ID NO:98)

Toxin Sequence:

Cys-Gln-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Asp-Cys-Cys-Gly-Xaa5-Cys-Val-Leu-Leu-Leu-Cys-Ile-[^] (SEQ ID NO:99)

Name: Omaria7
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

TTTTGAAGCNGGTACGCCTGCAGGTACCGGTCCGGAATTCCTGGGTCGACATCATCA
 TCATCATCGATCCATCTGTCCATCCATCCATTCAATTCGCTACCAGACTGTAATA
 AATATTCGGGTCTCTCTTCTGTTGTATCTGACAGATTGGACAAGAGGTGCATTCC
 ACATTTTGACCCTTGTGACCCGATACGCCACACCTGCTGCTTTGGCCTGTGCCTACT
 AATAGCCTGCATCTAAAACCTGCCGTGATGTCTTCTCCTCCCTCTAGTAGTAGTAGG
 CGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTC
 TATAGTGTACCTAAATTCAATTCAGTGGCCGTCGTTTACAACGTCGTGACTGGGA
 AAACCTGGCGTTACCAACTTAATTCGCCTTGCAGCACATCCCCCTTTCGCCAGCTG

GCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGA
ATGGCGAATGGGACGCGCCCTGTAGCGGCGCT (SEQ ID NO:100)

Translation:

LDKRCIPHFDPDPIRHTCCFGLCLIACI (SEQ ID NO:101)

Toxin Sequence:

Cys-Ile-Xaa3-His-Phe-Asp-Xaa3-Cys-Asp-Xaa3-Ile-Arg-His-Thr-Cys-Cys-Phe-Gly-Leu-Cys-
Leu-Leu-Ile-Ala-Cys-Ile-[^] (SEQ ID NO:102)

Name: Omaria11

Species: omaria

Isolated: No

Cloned: Yes

DNA Sequence:

GGTACGCCGTCAGGTACCGGTCCGGAATTCCCGGGTCGACATCATCATCGATCC
ATCTGTCCATCCATCCTTTCATTGTGCGCAGACTGTAATAAATATTCGAGTCT
CTCTTTCTGTTTGTATCTGACAGATTGAACAAGAGGTGCCTTGAGTTTGGTGAAGTT
TGTAATTTTTTTTCCCAACCTGCTGCGGCTATTGCGTCTTCTTGCTGCGCTATAAA
ACTACCGTGATGTCTTCTTCCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGAT
CCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTCACCTAAAT
TCAATTCACCTGCGCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCC
AACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGG
CCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCG
CCCTGTAGCGGCGCATTAAG (SEQ ID NO:103)

Translation:

LNKRCLEFGEVCNFFFTCCGYCVLLVCL (SEQ ID NO:104)

Toxin Sequence:

Cys-Leu-Xaa1-Phe-Gly-Xaa1-Val-Cys-Asn-Phe-Phe-Phe-Xaa3-Thr-Cys-Cys-Gly-Xaa5-Cys-
Val-Leu-Leu-Val-Cys-Leu-[^] (SEQ ID NO:105)

Name: O6.5

Species: obscurus

Isolated: No

Cloned: Yes

DNA Sequence:

00221-256426

cgatccatctgtccatccatccattcgttcgttcgtgccaaactgtaataaataaccgagtcctctgtttgtatctgacagATCGAAAA
 AGCAATGCCGTCAAATGGTGAAGTGTGTGATGCGAATTTGGCACACTGCTGCAGT
 GGCCCCGTGTTTCTCTCTGTCTAAACCAGCCGTGATGCTTCTACTCCCCTC (SEQ
 ID NO:106)

Translation:

VSDRSKKQCRQNGEVCDANLAHCCSGPCFLFLNQP (SEQ ID NO:107)

Toxin Sequence:

Ser-Lys-Lys-Gln-Cys-Arg-Gln-Asn-Gly-Xaa1-Val-Cys-Asp-Ala-Asn-Leu-Ala-His-Cys-Cys-
 Ser-Gly-Xaa3-Cys-Phe-Leu-Phe-Cys-Leu-Asn-Gln-Xaa3-^ (SEQ ID NO:108)

Name: Af6.8
Species: ammiralis
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTT
 GCCACGGCTGATGACTCCGGAAATGGATTGGAAAATCTTTTTTCAAGGCACATCA
 CGAAATGAAGAACCCCAAAGCCTCTAAATTGAACAAGAGGTGCACTCAAAGCGGTG
 AACTTTGTGATGTGATAGACCCAGACTGCTGCAATAATTTTGCATTATATTTTCTG
 CATATAAACTGCCGTGATGCTTCTACTCCCCTC (SEQ ID NO:109)

Translation:

MKLTCVMILAVLFLTAWTFATADDSGNLENLFSKAHHMKPNKASKLNKRCTQSGEL
 CDVIDPDCNNFCIIFFCI (SEQ ID NO:110)

Toxin Sequence:

Cys-Thr-Gln-Ser-Gly-Xaa1-Leu-Cys-Asp-Val-Ile-Asp-Xaa3-Asp-Cys-Cys-Asn-Asn-Phe-Cys-
 Ile-Ile-Phe-Phe-Cys-Ile-^ (SEQ ID NO:111)

Name: KK-2A
Species: textile
Isolated: No
Cloned: Yes

DNA Sequence:

GGCATTACCTAAAACATCACCAAAATGAACTGACGTGCATGATGATCGTTGCTGT
 GCTGTTCTTGACCGCTGGACATTGCGCACGGCTGATGACTCCGGAAATGGATTGGA
 GAAACTTTTTTCGAATGCACATCACGAAATGAAGAACCCTCTAATTGGA
 ACAAGAGGTGCGCTCCTTTTCTTACCTTTGTACCTTTTCTTCCCAAATGCTGCAA
 CGGCTATTGCGTTCAATTATCTGCCTATAAACTACTGTGATGTCTTCTATTCCCT
 C (SEQ ID NO:112)

Translation:

10 MKLTCMMIVAVLFLTAWTFATADDSGNLEKLFNSNAHHMKNPEASNLNKRCAFLH
 LCTFFFPNCCNGYCVQFICL (SEQ ID NO:113)

Toxin Sequence:

15 Cys-Ala-Xaa3-Phe-Leu-His-Leu-Cys-Thr-Phe-Phe-Phe-Xaa3-Asn-Cys-Cys-Asn-Gly-Xaa5-Cys-
 Val-Gln-Phe-Ile-Cys-Leu-^ (SEQ ID NO:114)

Name: KKM1
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCTAGCACAGTGAATTTGGCTTCACAGTTTTCCACTGTCGTCTTTGGCATCATC
 CAAAACATCACCAAGATGAACTGACGTGCATGATGATCGTTGTGTGCTGTTCTTG
 ACCGCCTGGACATTTGCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTT
 TCGAAGGCACATCACGAAATGAAGAACCCTAAAGACTCTAAATTGAACAAGAGGT
 GCCTTGACGCTGGTGAAATGTGTGATCTTTTAATTCAAATGCTGCAGTGGGTGGT
 GCATTATCTCTCTGCGCATAAACTACCGTGATGTCTTCTACTCCCCCTCTGTGCTA
 CCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCTGATCC
 GACTCTCTGGCGGCTCGGGGGTTCAACATCCAAATAAAGCCGACACGATACTGAC
 GTAGAAAAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:115)

Translation:

MKLTCMMIVAVLFLTAWTFATADDPRNGLNLFNSKAHHMKNPKDSLNLNKRCLDAGE
 MCDLFNSKCCSGWCILFCA (SEQ ID NO:116)

Toxin Sequence:

Cys-Leu-Asp-Ala-Gly-Xaa1-Met-Cys-Asp-Leu-Phe-Asn-Ser-Lys-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Ile-Leu-Phe-Cys-Ala-^ (SEQ ID NO:117)

008221.4364660

Name: KKM4
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GCCGAAAACATCACCAAGATGAAACTGACGAGCATGATGATCGTTGCTGTGCTGTT
 CTTGACCGCCTGGACATTCTGTCACGGCTGACGACTCCGGAAATGGGAGAATC
 TTTTTCGAAGGCACATCACGAGATGAAGAACCCCAAAGACTCTAAATTGAACAAG
 AGGTGCCTTGACGGTGGTGAATTTGTGGTATTTTGTTCGAAGCTGCTGCAGTGCG
 TGGTGCATTGTTCTCGTCTGCGCATGAAACTACCGTGATGTCTTCTACTCCCCTCTGT
 GCTACCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCCCTG
 ATCCGACTCTCTGGCGGCCCTCGGGGTTCAACATCCAAATAAAGCGACACGACAAT
 GACAAAAAAAAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:118)

Translation:

MKLTSMIMIVAVLFLTAWTFVTADDSGNLENLFSKAHHHEMKNPKDSKLNKRCLDGGE
 ICGILFPSCSGWCIVLVCA (SEQ ID NO:119)

Toxin Sequence:

Cys-Leu-Asp-Gly-Gly-Xaa1-Ile-Cys-Gly-Ile-Leu-Phe-Xaa3-Ser-Cys-Cys-Ser-Gly-Xaa4-Cys-
 Ile-Val-Leu-Val-Cys-Ala-^ (SEQ ID NO:120)

Name: KKM5
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GCTAGCACAGTGAATTTGGCTTCACAGTTTCCACTGTCGCTTTTGGCATCATCCAA
 AACATCACCAAGATGAAACTGACGTGCATGATGATCGAAGCAGAGCTGTTCTTGAC
 CGCCTGGACATTTGCCACGGCTGATGACCCCGAGAAATGGATTGGAGAATCTTTTTTC
 GAAGGCACATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGC
 CCTAACACTGGTGAATTATGTGATGTGGTTGAACAAAACTGCTGCTATACCTATTGC
 TTTATTGTAGTCTGCCCTATATAACTACCGTGATGTCTTCTACTCCCCTCTGTGCTGC
 CTGGCTTGATCTTTGATTGGCGCGTGCCCTTCACTGGTTATGAACCCCCCTGATCCG
 ACTCTCTTGGCGGCTCAGGGGTTCAACATCCAAATAAAGCGACACGAAAATGAAAA
 AAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:121)

Translation:

MKLTCTMMIEAELFLTAWTFATADDPNGLNLFASKAHHEMKNPEASKLNKRCPNTGEL

00021-2361260

CDVVEQNCCYTYCFIVVCPI (SEQ ID NO:122)

Toxin Sequence:

- 5 Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-Cys-Phe-Ile-Val-Val-Cys-Xaa3-Ile-[^] (SEQ ID NO:123)

Name: KKM6
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

15 TTGCACGGTGAATTCGCTTATATTTTCTACTGTCGCTCTTGGCATCATCCAAAACA
 TCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCT
 GGACATTCGTACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTTTATCTGA
 20 AGGCACCTCACGAAACGGAAAACCAAGCCTCTAAATTGAACGTGAGAGACGA
 CGAGTGCGAACCTCCTGGAGATTTTGTGGCTTTTTAAAAATTGGGCCGCCCTTGCTG
 CAGTGGCTGGTGCTTCTCTGGTGCGCCTAAAACCTGCCGTGATGTCCTTATTCCTCT
 CTGTGCTACCTGGCTGATCTTTGATTGGCGCGTGCCCTTCAGTGTTATGAACCCCT
 CTGATCCGACTCTCTGGGGGCCCTCGGGGGTTCAACATCCAAATAAAGCTGACAACA
 CAATAAAAAAAAAA (SEQ ID NO:124)

Translation:

MKLTCMMIVAVLFLTAWTFVTAAPHSSDVLENLYLKALHETENHEASKLNVRDDECEP
 PGDFCGFFKIGPPCCSGWCFWLCA (SEQ ID NO:125)

Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-[^] (SEQ ID NO:126)

Name: C. striatus S2
Species: striatus
Isolated: No
Cloned: Yes

DNA Sequence:

45 ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGTGCCTCACTCCAGCGATGATTGGAGAATCTTTATCTGAAGGCACTT
 CACGAAACGGAAAACCAAGCCTCTAAATTGAACGTGAGAGACGACGAGTGCG
 AACCTCCTGGAGATTTTGTGGCTTTTTAAAAATTGGGCCGCCCTTGCTGCAGTGGCT

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GGTGCTTCTCTGGTGCGCATAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:127)

Translation:

MKLTCVMIVAVLFLTAWTFVTAVPHSSDALENLYLKALHETENHEASKLNVRDDECEP
PGDFCGFFKIGPPCCSGWCFLWCA (SEQ ID NO:128)

Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-
Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-^ (SEQ ID NO:129)

Name: Om6.5
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAAAATCTTATCTGAAGGCACGT
CACGAAATGGAAAACCCCGAAGCCTCTAAATTGAACACGAGAGACGACGATTGCG
AACCTCCTGGAATTTTTGTGGCATGATAAAAATTGGCCGCCTTGCTGCAGTGGCT
GGTGCTTTTTTCGCTGCGCCTAAAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID
NO:130)

Translation:

MKLTCVMIVAVLFLTAWTFVTAVPHSSNALENLYLKHARHEMENPEASKLNTRDDDCPE
PGNFCGMIKIGPPCCSGWCFFACA (SEQ ID NO:131)

Toxin Sequence:

Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-
Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:132)

Name: Au6.3
Species: aulicus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATAGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC

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GTCACGGCTGTGCCTCACTCCAGCAATGCATTGGAGAATCTTTATCTGAAGGCACGT
 CACGAAATGGAAAACCCCGAAGCCTCTAAATTGAACACGAGAGACTACGATTGCGA
 ACCTCCTGGAAATTTTTGTGGCATGATAAAAATTGGCCCGCTTGCTGCAGTGGCTG
 GTGCTTTTTCGCCTGCGCCTAAAACCTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID
 NO:133)

Translation:

MKLTCLMIVAVLFLTAWTFVTVAPHSSNALENLYLKARHEMENPEASKLNTRDYDCEP
 PGNFCGMKIGPPCCSGWCFFACA (SEQ ID NO:134)

Toxin Sequence:

Asp-Xaa5-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:135)

Name: Marm9
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCATCATCGATCCATCTGTCCATCCATCTATTCATTTCATTTCGTG
 GCCAAACTGTAATAAATAATGCAAGTCTCTCTTTCTGTTTGTATCTGACAGATTGAA
 CACGAGAGACGACGATTGCGAACCTCCTGGAAATTTTGTGGCATGATAAAAATTG
 GGCCGCGCTTGCTGCAGTGGCTGGTCTTTTCGCCTGCGCCTAAAACCTGCCGTGATG
 TCTTCTCTTCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGT
 ACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTACCTAAATTCATTCACCTGG
 CCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTACCCAATTAATCGCC
 TTGCAGACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGAT
 CGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGG
 CGCATTAAAGCGCGCGGGGTGTGGTGGTTACGCCCGAGCCGTGACCCGCTACACTTG
 CCAGCGCCCTAGCGCCCGCTCCTTTTCGCTTTCTTCCTTCTCCTTCGCGCACGTTTCGCC
 GGCTTTTCCCGTCAAGCTCTAAATCGGGGGCTCCTTTAGGGTCCGATTTAAGTGCTT
 TAC (SEQ ID NO:136)

Translation:

LNTRDDDDCEPPGNFCGMKIGPPCCSGWCFFACA (SEQ ID NO:137)

Toxin Sequence:

Asp-Asp-Asp-Cys-Xaa1-Xaa3-Xaa3-Gly-Asn-Phe-Cys-Gly-Met-Ile-Lys-Ile-Gly-Xaa3-Xaa3-
 Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Ala-Cys-Ala-^ (SEQ ID NO:138)

09749637-122800

Name: Rg6.4
Species: regius
Isolated: No
Cloned: Yes

DNA Sequence:

TTGAACCAGAGAGACTGCCTTAGTAAAAACGCTTCTGTGCCTGGCCGATACTTGGA
 CCACTGTGCTGCAGTGGCTGGTGCCTATACGTCTGCATGTAAAACTGCCGTGATGTC
 TTCTATCCCCTC (SEQ ID NO:139)

Translation:

LNQRDCLSKNAFCAWPILGPLCCSGWCLYVCM (SEQ ID NO:140)

Toxin Sequence:

Asp-Cys-Leu-Ser-Lys-Asn-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-
 Gly-Xaa4-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:141)

Name: R6.5
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATTGAACAAGAAAGGTGATGACTGCCTTGCTGTAAAAAAATTGTGGCTTTCCAA
 AACTTGGAGGCCCATGCTGCAGTGGCTTGCTTTTCGTCTGCGCCTAAAACTGCC
 GTGATGTCTTCTCCTCCCCT (SEQ ID NO:142)

Translation:

LNKKGDDCLAVKKNCGFPKLGGPCCSGLCFFVCA (SEQ ID NO:143)

Toxin Sequence:

Gly-Asp-Asp-Cys-Leu-Ala-Val-Lys-Lys-Asn-Cys-Gly-Phe-Xaa3-Lys-Leu-Gly-Gly-Xaa3-Cys-
 Cys-Ser-Gly-Leu-Cys-Phe-Phe-Val-Cys-Ala-^ (SEQ ID NO:144)

Name: Rg6.2
Species: regius
Isolated: No

Cloned: Yes

DNA Sequence:

5 TTGAATCAGAGCGACTGCCTTCCTAGAGACACATTCTGTGCCTTGCCGCAACTTGGA
CTACTGTGCTGCAGTGGCCGGTGCTTACTCTTCTGCGTGTAAACTGCCGTGATGTC
TTCTCTCCCCCTC (SEQ ID NO:145)

Translation:

10 LNQSDCLPRDTFCALPQLGLCCSGRCLLFCV (SEQ ID NO:146)

Toxin Sequence:

15 Asp-Cys-Leu-Xaa3-Arg-Asp-Thr-Phe-Cys-Ala-Leu-Xaa3-Gln-Leu-Gly-Leu-Leu-Cys-Cys-Ser-
Gly-Arg-Cys-Leu-Leu-Phe-Cys-Val-^ (SEQ ID NO:147)

Name: A6.5
Species: aurisiacus
Isolated: No
Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGCGTGATGACCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTTCCGAAGGCACGTCA
TGAAATGAAGAACCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAATG
CTGGTGCATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGATTTCATTGTTT
30 GGTGCACATGAGTCGTATTCTGCTGGTACATTTTGTGGCTTCAACGGAGGACTCTGC
TGCAGCAACCTTTGCTTATTTTTCGTGTGCTTAACATATTCGTGATGTCTTCTACTCC
CATC (SEQ ID NO:148)

Translation:

35 MKLTCVMTVAVLFLTAWTFVTADDSRNLKNLFPKARHEMKNPEASKLNKRDGCSNA
GAFCGIHPGLCCSEICIVWCT (SEQ ID NO:149)

Toxin Sequence:

40 Asp-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Ile-
Cys-Ile-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:150)

45 **Name:** δ-PVIA
Species: purpurascens
Isolated: Yes

00821-2694260

Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA
 CGAAATGAAGAACC CGGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATGCCG
 CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTTTGTCTCCCG
 10 GCGTCTGCTTCGGTGGTTAACTGCCGTGATGTCTTCTACTCCCCTCTGTGCTACCTGG
 CTTGATCTTTGATCGGCGTGTGCCCTTCACTGGTTATGAACCCACTGATCTTACCTCT
 CTTGAAGGACCTCTGGGGTCCAGCATCCAAATAAGCGACATCCCAATGAAAAAAAA
 AAAAAAAAAAAAAA (SEQ ID NO:151)

Translation:

15 MKLTCVMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDKKEACYA
 PGTFCGIKPGLCCSEFLPGVCFGG (SEQ ID NO:152)

Toxin Sequence:

20 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-# (SEQ ID NO:153)

25 **Name:** δ-PVIA-OH
Species: purpurascens
Isolated: Yes

Toxin Sequence:

30 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:153)

35 **Name:** δ-PVIA[F9A]
Species: purpurascens

Toxin Sequence:

40 Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Ala-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:154)

45 **Name:** δ-PVIA[I12A]
Species: purpurascens
Isolated:

09749537.122800

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Thr-Phe-Cys-Gly-Ala-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:155)

Name: δ -PVIA[T8A]
Species: purpurascens

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Ala-Xaa3-Gly-Ala-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Leu-Xaa3-Gly-Val-Cys-Phe-Gly-^ (SEQ ID NO:156)

Name: M6.3
Species: magus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT
 GAAATGAAGAACCCCTGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTATAATGC
 TGGTACATTTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTTGCTTTTTATGG
 TGCATAACATTTGTTGATTCTGGCTAACAGTGTGCGTTGGTTAGTGTCTTCTCCTCCC
 CTC (SEQ ID NO:157)

Translation:

MKLTCVMIVAVLFTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDCGCYNA
 GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:158)

Toxin Sequence:

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:159)

Name: M6.6
Species: magus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC
 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTTCCGAAGGCACGTCAT
 GAAATGAAGAACCCTGAAGCCTCTAAATTGAACAAGAGAGATGAATGCTATCCTCC
 TGGTACATTTTGTGGCATCAAAACCAGGACTTTGCTGCAGCGCGATATGCTTATCGTT
 TGCTGCATATCATTTGATTGTTTTGATTGATGCTTCTCTCCTCCCTC (SEQ ID NO:160)

Translation:

MKLTCVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRDECYP
 P (SEQ ID NO:161)

Toxin Sequence:

Asp-Xaa1-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Ala-Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe-^ (SEQ ID NO:162)

Name: M6.7
Species: magus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTACTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTCCGAAGGAACGTC
 TGAATGAAGAACCCTGAAGCCTCTAAATTGAACCAGAGAGAAGCCTGCTATAATG
 CTGGTTCAATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGCATTCTTTG
 GTGCATAACATTTGTTGATTCTGGCTAACTGTGTGCGTTGGTTGATGCTTCTCTCC
 CATC (SEQ ID NO:163)

Translation:

MKLTCVMIVAVLFLTAWTFVTADDSRYGLKDLFPKERHEMKNPEASKLNQREACYN
 A (SEQ ID NO:164)

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Ser-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Phe-Cys-Ile-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:165)

Name: M6.8
Species: magus
Isolated: No
Cloned: Yes

008221-26964260

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTACTGTTCTTGACCGCCTGGACATTC
 5 GTCACGGCTGATGACTCCAGATATGGACTGAAGGATCTGTTTCCGAAGGAACGTCA
 TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGAGAGAAAGCCTGCTATAATG
 CTGGTACATTTTGTGGCATCAAACCAAGGACTTGTGCAGCGCGATATGCTTATCGT
 TTGTCTGCATATCATTTGATTTTGTATTGATGTCTTCTCTCCCTC (SEQ ID NO:166)

Translation:

10 MKLTCMMIVAVLFLTAWTFVTADDSRYGLKDLFPKERHEMKNPEASKLNQREACYNA
 GTFCGIKPLGCCSAICLSFVCISFDF (SEQ ID NO:167)

Toxin Sequence:

15 Xaa1-Ala-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Ala-
 Ile-Cys-Leu-Ser-Phe-Val-Cys-Ile-Ser-Phe-Asp-Phe- (SEQ ID NO:168)

20 **Name:** E6.4
Species: ermineus
Isolated: No
Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC
 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC
 30 CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTGTGTTTACCGG
 CCGTCTGCGTCCGGTGTTAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:169)

Translation:

35 MKLTCVMIVAVLFLTAWTFVTADDSKNGLNHFWKARDEMKNREASKLDKKEACYP
 PGTFCGIKPLCCSELCLPAVCVGG (SEQ ID NO:170)

Toxin Sequence:

40 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:171)

45 **Name:** P6.4
Species: purpurascens
Isolated: No
Cloned: Yes

000221-22964760

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC
 5 GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA
 CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGG
 CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTGTGTTTACCGG
 CCGTCTGCGTCGGTGTTAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:172)

Translation:

MKLTCTMMIVAVLFLTAWTFVTADDSKNLENHFWKARDEMKNREASKLDKKEACYP
 PGTFCGIKPGLCCSELCLPAVCGVG (SEQ ID NO:173)

Toxin Sequence:

Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
 Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:174)

Name: δ-SVIE [D1E]
Species: striatus
Isolated: Yes
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCCTTGACATTC
 25 GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTTCCGAAGGCACGTCAT
 30 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGAAGGGTGCTCTAGTG
 GTGGTACATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTGTCTTCTTTG
 GTGCATAACATTTATTGATTGATGTCTTCTCTCCCTC (SEQ ID NO:175)

Translation:

MKLTCTVMIVAVLFLTTWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKREGCSSG
 GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:176)

Toxin Sequence:

Xaa1-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:177)

Name: δ-SVIE
Species: striatus
Isolated: Yes

008221-2594760

Cloned: Yes

DNA Sequence:

5 ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCACTTGGACATTC
GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGG
TGGTACATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGTTTTGCTTTCTTTGG
TGCATAACATTTATTGATTGATGTCTTCTCCTCCCCTC (SEQ ID NO:178)

Translation:

MKLTCVMIVAVLFLTWTFTVTTADDSRYGLKNLFPKARHEMKNPEASKLNKRDGCSSG
GTFCGIHPGLCCSEFCFLWCITFID (SEQ ID NO:179)

Toxin Sequence:

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-[^] (SEQ ID NO:180)

Name: δ-NgVIA
Species: striolatus
Isolated: Yes

Toxin Sequence:

Ser-Lys-Cys-Phe-Ser-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-Val-
Arg-Cys-Phe-Ser-Leu-Phe-Cys-Ile-Ser-Phe-Xaa1-[^] (SEQ ID NO:181)

Name: C6.2
Species: catus
Isolated: No
Cloned: Yes

DNA Sequence:

40 ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGATGACTCCAGAAATGGACTGAAGAATCTTTTCCGAAGGCACGTCA
TGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGATATGGGTGCTCTAATG
CTGGTGCAATTTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTTGCCTGGTTT
GGTGCACATGAGTGCTATTCTTCTGGTACATTTTGTGGCTTCAACGGAGGACTCTGC
TGCAGCAACCTTTGCTTATTTTCGTGTGCTTAACATTTTCGTGATGTCTTCTCTATTCC
45 CCTC (SEQ ID NO:182)

Translation:

09749637-122806

MKLT CMMIVAVLFLTAWTFVTADDSRNLGNLFPKARHEMKNPEASKLNKRYGCSNA
GAFCGIHPGLCCSELCLVWCT (SEQ ID NO:183)

5 Toxin Sequence:

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Leu-Cys-Leu-Val-Xaa4-Cys-Thr-^ (SEQ ID NO:184)

Name: C6.3
Species: catus
Isolated: No
Cloned: Yes

15 DNA Sequence:

ATGAAACTGACGTGTATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGATGACTCCAGATATGGACTGAAGAATCTTTTTCCGAAGGCACGTCAT
20 GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGATATGGGTGCTCTAATGC
TGGTGCAATTTGTGGCATCCATCCAGGACTCTGCTGCAGCGAGCTTTGCCTGGGTG
GTGCACATGAGTGCTATTCTACTGGTACATTTTGTGGCTTCAACGGAGGACTCTGCT
GCAGCAACCTTTGCTTATTTTCGTGTGCTTAACATTCGTGATGTCTTCTATTCCC
CTC (SEQ ID NO:185)

25 Translation:

MKLT CMMIVAVLFLTAWTFVTADDSRYGLKNLFPKARHEMKNPEASKLNKRYGCSNA
GAFCGIHPGLCCSELCLGWCT (SEQ ID NO:186)

30 Toxin Sequence:

Xaa5-Gly-Cys-Ser-Asn-Ala-Gly-Ala-Phe-Cys-Gly-Ile-His-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Leu-Cys-Leu-Gly-Xaa4-Cys-Thr-^ (SEQ ID NO:187)

Name: Di6.3
Species: distans
Isolated: No
Cloned: Yes

40 DNA Sequence:

ATGAAACTGACGTGTCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
45 GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTCTCTCCGAAGGCACCTCA
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAAGAGATATGAGTGCTATCTAC
TGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT

CGTGTGCTTAACATTTTCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:188)

Translation:

- 5 MKLTCLMIVAVLFLTAWTFVTADDSRNGLENLSPKAPHEMKNPASKSNKRYECYLLV
HFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:189)

Toxin Sequence:

- 10 Xaa5-Xaa1-Cys-Xaa5-Leu-Leu-Val-His-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:190)

Name: Rg6.1
Species: regius
Isolated: No
Cloned: Yes

DNA Sequence:

TTGAGCAAGAGAGACTGCCTTCCTGACTACACGATTTGTGCCTTCAATATGGGTCTG
TGCTGCAGCGACAAGTGCATGCTCGTCTGCCTGCCGTGATGTCTTCTCCTCCCTC
(SEQ ID NO:191)

Translation:

LSKRDCLPDYTICAFNMGLCCSDKCMLVCLP (SEQ ID NO:192)

Toxin Sequence:

Asp-Cys-Leu-Xaa3-Asp-Xaa5-Thr-Ile-Cys-Ala-Phe-Asn-Met-Gly-Leu-Cys-Cys-Ser-Asp-Lys-
Cys-Met-Leu-Val-Cys-Leu-Xaa3-^ (SEQ ID NO:193)

Name: Rg6.3
Species: regius
Isolated: No
Cloned: Yes

DNA Sequence:

TTGAACAAGAGAATCATCTGCTTTTCCTGACTACATGTTTTGTGGCGTCAATGTGTTTC
TGTGCTGCAGTGGCAACTGCCTTCTCATCTGCGTGCCGTGATGTCTTCTACTCCCTC
(SEQ ID NO:194)

Translation:

LNKRIICFPDYMFCGVNVFLCCSGNCLLCVP (SEQ ID NO:195)

Toxin Sequence:

- 5 Ile-Ile-Cys-Phe-Xaa3-Asp-Xaa5-Met-Phe-Cys-Gly-Val-Asn-Val-Phe-Leu-Cys-Cys-Ser-Gly-Asn-Cys-Leu-Leu-Ile-Cys-Val-Xaa3-^ (SEQ ID NO:196)

Name: Gm6.2
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGTGCCCTCACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT
 CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG
 GACAGGTTGTGACTCTGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGCCTGCCT
 CTAAAACTGTCTGATGTCTTCTCCTCCCTC (SEQ ID NO:197)

Translation:

MKLTMMIVAVLFLTAWTFVTAIPHSSNALENLYLKAHHEMNPNPESELNKRCYDGG
 TGCDSGNQCCSGWCIFACL (SEQ ID NO:198)

Toxin Sequence:

Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-Phe-Ala-Cys-Leu-^ (SEQ ID NO:199)

Name: Da6.1
Species: dalli
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATTATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGTGCCCTCACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT
 CATGAAATGAACAACCCCGAGGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG
 GACAGGTTGTGACTCTGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGTCTGCCT
 CTAAAACTGCCGTGATGTCTTCTCTCCCATC (SEQ ID NO:200)

Translation:

MKLTCIMIVAVLFLTAWTFVTVAPHSSNALENLYLKAHHEMNPNPESELNKRCDGGT
GCDSGNQCCSGWCIFVCL (SEQ ID NO:201)

Toxin Sequence:

5

Cys-Xaa5-Asp-Gly-Gly-Thr-Gly-Cys-Asp-Ser-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Val-Cys-Leu-^ (SEQ ID NO:202)

10 **Name:** Pn6.6
Species: pennaceus
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACAGTC
GTCACGGCTGTGCCTCACTCCAACAAGCGGTTGGCGAATCTTTATCTGAAGGCACGT
CACGAAATGAAAAACCCGAAGCCTCTAATGTGGACAAGAGGTGCTTTGAGAGTTG
GGTAGCTTGTGAGTCTCCAAACGATGCTGCAGTCACGTGTGCCTTTTCGTCTGCAC
CTGAAACTGCCGTGATGTCTTCTCCTCCCTC (SEQ ID NO:203)

Translation:

25 MKLTCVMIVAVLFLTAWTVVTAVPHSNKRLANLYLKARHEMNKNPEASNVDKRCFESW
VACESPKRCCSHVCLFVCT (SEQ ID NO:204)

Toxin Sequence:

30 Cys-Phe-Xaa1-Ser-Xaa4-Val-Ala-Cys-Xaa1-Ser-Xaa3-Lys-Arg-Cys-Cys-Ser-His-Val-Cys-Leu-
Phe-Val-Cys-Thr-^ (SEQ ID NO:205)

35 **Name:** Di6.5
Species: distans
Isolated: No
Cloned: Yes

DNA Sequence:

40

ATGAAACTGACGTGTATGTTGATCATCGCTGTGCTGTTCTGACGGCCTGTCAACTC
TCTACAAATGCGAGTTACGCCAGAAGTAAGCAGAAGCATCGTGTCTGAGGTCGAC
TGACAAAACTCCAAGTTGACCCAGCGTTGCAATGAAGCTCAAGAACATTGCACCT
AAAATCCTGACTGCTGCAGTGAGTCTTGCAATAAGTTTGTGGCAGATGCTTGTGAC
45 ACTGATCTGATGTCTTCTCTCCCATC (SEQ ID NO:206)

Translation:

008221-12964260

MKLTCMLIIAVLFLTACQLSTNASYARSKQKHRVLRSTDKN SKLTQRCNEAQEHCTQN
PDCCSESCNKFVGRCLSD (SEQ ID NO:207)

5 **Toxin Sequence:**

Cys-Asn-Xaa1-Ala-Gln-Xaa1-His-Cys-Thr-Gln-Asn-Xaa3-Asp-Cys-Cys-Ser-Xaa1-Ser-Cys-
Asn-Lys-Phe-Val-Gly-Arg-Cys-Leu-Ser-Asp-^ (SEQ ID NO:208)

10

Name: Af6.10
Species: ammiralis
Isolated: No
Cloned: Yes

15

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTCTTACCGCCTGGACATTCTC
GTCACGGCTGTGCCTGACTCCAGCAATGCGTTGGAGAATCTTTATCTGAAGGCACAT
CATGAAATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATGGTGG
GACAAGTTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCTCTGCCT
CTAAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:209)

20

Translation:

MKLTCMLIVAVLFLTAWTFVTAVPDSSNALENLYLKAHHEMNPNPEDSELNKRCDYDGG
TSCNTGNQCCSGWCIFLCL (SEQ ID NO:210)

25

Toxin Sequence:

Cys-Xaa5-Asp-Gly-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
Phe-Leu-Cys-Leu-^ (SEQ ID NO:211)

30

35 **Name:** Tx6.10
Species: textile
Isolated: No
Cloned: Yes

40 **DNA Sequence:**

GGCATTACCTAAAACATCACCAAGATGAAACTGACGTGCATGATGATCGTTGCTGT
GCTGTTCTTGACCGCCTGGACATTCTGTCACGGCTGCGCCTCACTCCAGCAATGCGTT
GGAGAATCTTTATCTGAAGGCACATCATGAAATGAACAACCCCGAAGCCTCTGAAT
45 TGAACAAGAGGTGCTATGATAGTGGGACAAGTTGTAACACTGGAAACCAATGCTGC
AGTGGCTGGTGCATTTTCTGCTCTTGCCTCTAAAACTACCGTGATGTCTTCTCCTCCC
CTC (SEQ ID NO:212)

45

09749637.122800

Translation:

MKLTMMIVAVLFLTAWTFVTAAPHSSNALENLYLKAHHEMNNPASELNKRCYDSG
 5 TSCNTGNQCCSGWCIFVSCL (SEQ ID NO:213)

Toxin Sequence:

Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
 10 Phe-Val-Ser-Cys-Leu-^ (SEQ ID NO:214)

Name: Gm6.4
Species: gloriamaris
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTGACAGCCTGGACGCTA
 20 GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCTTTTTTCGAAATCACGTGAC
 GAAATGGAGGACCCCGAAGCTTCTAAATTGGAGAAAAGGGATTGCCAAGCACTATG
 GGATTATTGTCCAGTACCGCTCTTGTGCATCGGGTGATTGCTGCTATGGCTTAATCTGT
 25 GGCCCTTTCGTCTGCATTGGATGGTGATGTCTTCTACTCCCATC (SEQ ID NO:215)

Translation:

MKLTMMIVAVLFLTAWTLVMADDSNNGLANLFSKSRDEMEDPEASKLEKRDCQAL
 30 WDYCPVPLLSSGDCCYGLICGPFVCIGW (SEQ ID NO:216)

Toxin Sequence:

Asp-Cys-Gln-Ala-Leu-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Leu-Leu-Ser-Ser-Gly-Asp-Cys-
 35 Cys-Xaa5-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Ile-Gly-Xaa4-^ (SEQ ID NO:217)

Name: Om6.2
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 45 GTCATGGCTGATGACTCCAACA^TTG^GACTGGCAAATCTTTTTTCGAAATCACGTGAC
 GAAATGGAGGATACCGATCCTTCTAAATTGGAGAACAGAAAAA^CTGCCAAAGAG
 GTGGGATTTTTGTCCAGGATCGCTCGTTGGAGTGATAACTTGCTGCGGTGGCTTAAT

CTGTTTTCTGTTCTTCTGCGTTTGATAGTGATGCTCTTCTCTCCCCCT (SEQ ID NO:218)

Translation:

MKLTCLMIVAVLFLTAWTFVMADDSNNGLANLFSKSRDEMEDTDP SKLENRKT CQRR
WDFCPGSLVGVITCCGGLICFLFFCV (SEQ ID NO:219)

Toxin Sequence:

Lys-Thr-Cys-Gln-Arg-Arg-Xaa4-Asp-Phe-Cys-Xaa3-Gly-Ser-Leu-Val-Gly-Val-Ile-Thr-Cys-
Cys-Gly-Gly-Leu-Ile-Cys-Phe-Leu-Phe-Phe-Cys-Val-^ (SEQ ID NO:220)

Name: Da6.3
Species: dalli
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTGACAGCCTGGACGCTA
GTCATGGCTGATGACTCCAAACAATGGACTGGCGAATCTTTTTTCGAAATTACGTGAC
GAAATGGAGGACCCCGAAGGTTCTAAATTGGAGAAAAAGGATTGCCAAGAAAAAT
GGGATTATTGTTCCAGTACCGTTCTTGGGATCGAGGTATTGCTGCGATGGCTTTATCT
GTCCATCTTTCTTCTGCGCTTGATAGTGATGTCTTCTATTCCTC (SEQ ID NO:221)

Translation:

MKLTCLMIVAVLFLTAWTLVMADDSNNGLANLFSKLRDEMEDPEGSKLEKKDCQEK
WDYCPVPFLGSRYYCCDGFICPSFFCA (SEQ ID NO:222)

Toxin Sequence:

Asp-Cys-Gln-Xaa1-Lys-Xaa4-Asp-Xaa5-Cys-Xaa3-Val-Xaa3-Phe-Leu-Gly-Ser-Arg-Xaa5-Cys-
Cys-Asp-Gly-Phe-Ile-Cys-Xaa3-Ser-Phe-Phe-Cys-Ala-^ (SEQ ID NO:223)

Name: Da6.7
Species: dalli
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGTTGTTCTGACAGCCTGGACGCTA

00221.4694637.122800

GTCATGGCTGATGACTCCAACAATGGACTGGCGAATCATTTTTGGAAATCACGTGAC
GAAATGGAGGACCTGAAGCTTCTAAATTGGAGAAAAGGGATTGCCAAGGCGAATG
GGAGTTTTGTATAGTACCGTCTTGGATTGTGTATTGCTGCCCTGGCTTATCTGT
GGCCCTTCGTCGTCTGCGTTGATATCTGATGTCTTCTATCCCTC (SEQ ID NO:224)

Translation:

MKLTCEMIVAVLFLTAWTLVMADDSNNGLANHFWKSRDEMEDPEASKLEKRCQGE
WEFCIVPVLGFVYCCPWLICGPFVCVDI (SEQ ID NO:225)

Toxin Sequence:

Asp-Cys-Gln-Gly-Xaa1-Xaa4-Xaa1-Phe-Cys-Ile-Val-Xaa3-Val-Leu-Gly-Phe-Val-Xaa5-Cys-
Cys-Xaa3-Xaa4-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-Asp-Ile-^ (SEQ ID NO:226)

Name: Ph6.5
Species: pennaceus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCATTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCATGGCTGATGACCCAGAGATGAACCGGAGGCACGTGACGAAATGAACCCCGC
AGCCTCTAAATTGAACGAGAGAGGCTGCCTTGAAGTTGATTATTTTTCGGCATACC
GTTTGTGAACAACGGGCTATGCTGCAGTGGCAATTGTGTTTTGTCTGCACACCCCA
AGGGAAGTAAACTGCTGTGATGTCTTCTCTCCCATC (SEQ ID NO:227)

Translation:

MKLTCLMIAVLFLTAWTFVMADDPREDEPEARDEMNPAAASKLNERGCLEVDYFCGIPF
VNGLCCSGNCVFVCTPQ GK (SEQ ID NO:228)

Toxin Sequence:

Gly-Cys-Leu-Xaa1-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-
Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:229)

Name: Marm6
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GGTCGACATCATCATCGATCCATCTGTCCATCCATCTGTCCATCCATCCATTCAT
TCATTCACGTGCCAAACTGTCATAAAATATTGAGTCTCTCTTTCTGTTTTATCTGACA
GATTGAACGAGAGAGACTGCCCTTAATGTTGATTATTTTGCGGCATACCGTTTGGA
ACAACGGGCTATGCTGCAGTGGCAATTGTGTTTTGTCTGCACACCCCAAGGGAAGT
5 AAAACTGCCGTGATGTCTTCTCTTCCCCTCTAGTAGTAGTAGGCGGCCGCTCTAGAG
GATCCAAGCTTACGTACGCGTGCATGCGACGTACAGCTCTTCTATAGTGTACACCTA
AATTCAATTCACTGGCCGTCGGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTT
ACCCAACCTAATCGCCTTGCAGCACAT (SEQ ID NO:230)

10 Translation:

NERDCLNVDYFCGIPFVNGLCCSGNCVFVCTPQ GK (SEQ ID NO:231)

Toxin Sequence:

Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-Ser-
Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:232)

Name: Marm15
Species: marmoreus
Isolated: No
Cloned: Yes

25 DNA Sequence:

TCGACATCATCATCATCGATCCATCTGTCCATCCATCCATTCATTTCATTCGCTGCCAA
ACTGTCATAAAATATTGAGTCTCTCTTTCTGTTTTATCTGACAGATTGGACAAGAGA
GAGTGCCCTGGAAGCTGATTATTATTGCGTCTTACCGTTTGTGGGCAACGGGATGTGC
30 TGCAGTGGCATTGTGTTTTGTCTGCATAGCCC (SEQ ID NO:233)

Translation:

LDKRECLEADYYCVLPFVGNGMCCSGICVFVCIQRFKTV (SEQ ID NO:234)

Toxin Sequence:

Xaa1-Cys-Leu-Xaa1-Ala-Asp-Xaa5-Xaa5-Cys-Val-Leu-Xaa3-Phe-Val-Gly-Asn-Gly-Met-Cys-
Cys-Ser-Gly-Ile-Cys-Val-Phe-Val-Cys-Ile-Ala-Gln-Arg-Phe-Lys-Thr-Val-^ (SEQ ID NO:235)

Name: Marm10
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GTACCGGTCCGGAATTCCCGGGTCGACATCATCATCATCGATCCATCTGTCCATCCA
 TCCATCCATTCAATTCATTCGCTGCCAAACTGTCATAAAACATTTGAGTCTCTCTTTCTG
 TTTTATCTGACAGATTGAACGAGAGAGACTGCCTTGAACTGATTATGTTTGC GGC
 5 ATACCGTTTGTGTTCAACGGGCTATGCTGCAGTGGAATTTGTGTTTTATCTGCATAG
 CCCAAAAGTATTAACGCGGTGATGCTTCTATTCCCATCTAGTAGTAGTAGGCGG
 CCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTAT
 AGTGTACCTAAATTCAATTCACCTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAA
 CCCTGGCGTTACCCAACCTAATCGCCTTGACGACATCCCCCTTTCGCCAGCTGGCG
 10 TAATAGCCGAAGAGGCCCGACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAAT
 GGCGAATGGGG (SEQ ID NO:236)

Translation:

15 LNERDCLPEPDYVCGIPFVFNGLCCSGICVFICIAQKY (SEQ ID NO:237)

Toxin Sequence:

Asp-Cys-Leu-Xaa1-Xaa3-Asp-Xaa5-Val-Cys-Gly-Ile-Xaa3-Phe-Val-Phe-Asn-Gly-Leu-Cys-
 20 Cys-Ser-Gly-Ile-Cys-Val-Phe-Ile-Cys-Ile-Ala-Gln-Lys-Xaa5-^ (SEQ ID NO:238)

Name: Marm14
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

GGTACGCCTGCAGGTACCGGTCCGGAATCCCGGGTCGACATCATCATCATCGA
 TCCATCTGTCCATCCATCTATTCAATTCATTCGCTGTCAAACCTGTAATACATATTAGAA
 TCTCTCTTGTGTTGTATCTGACAGATTGGAGAAAAGGGCGTGCAGCAAAAAATGG
 GAATATTGTATAGTACCGATCCTTGGATTGATATTGCTGCCCTGGCTTAATCTGTG
 GTCCTTTCGCTGCGTTTGATAGTGATGCTTCTCCTCCCATCTAGTAGTAGTAGGCG
 35 GCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTA
 TAGTGTACCTAAATTCAATTCACCTGGCCGTCGTTTTACAACGTCGTGACTGGGAAA
 ACCCTGGCGTTACCCAACCTAATCGCCTTGACGACATCCCCCTTTCGCCAGCTGGC
 GTAATAAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAA
 TGGCGAAATGGGACGCGCCCTG (SEQ ID NO:239)

Translation:

LEKRACSKKWEYICVPIILGFVYCCPGLICGPFVVCV (SEQ ID NO:240)

Toxin Sequence:

Ala-Cys-Ser-Lys-Lys-Xaa4-Xaa1-Xaa5-Cys-Ile-Val-Xaa3-Ile-Leu-Gly-Phe-Val-Xaa5-Cys-Cys-

09749637.12800

Xaa3-Gly-Leu-Ile-Cys-Gly-Xaa3-Phe-Val-Cys-Val-[^] (SEQ ID NO:241)

Name: Omaria14
Species: omaria
Isolated: No
Cloned: Yes

DNA Sequence:

AAAGCCGGTACGCCCTGCAGGTACCGGTCCGGAATTCCTGGGTCGACATCATCATCA
 TCATCGATCCATCTGTCCATCCATCCATTCAATTCATCTGCCAAACTGTCATAAAT
 ATTTGAGTCTCTCTTTCTGTTTTATCTGACAGATTGAACGAGAGAGACTGCCTTAAT
 GTTGATTATTTTGTGGCATAACCGTTTGTGAACAACGGGCTATGCTGCAGTGGCAAT
 TGTGTTTTTTGTCTGCACACCCCAAGGGAAGTAACTGCCGTGATGCTCTTCTCTTCC
 CCTCTAGTAGTAGTAGGCGGCCGCTCTAGAGGATCCAAGCTTACGTACGCGTGCA
 TGGCAGCTCATAGCTCTTCTATAGTGTACCTAAATCAATTCAGTGGCCGTGTTTTA
 CAACGTCGTGACTGGGAAAACCTGGCGTTACCCAACCTAATCGCCTTGCAGCACAT
 CCCCCTTCGCGCAGCTGGCGTAATAGCGAAGAGGCCCGCACCCGATCGCCCTCCCA
 ACAGTTGCGCAGCCTGAATGGCGAATGGGACGCGCCCT (SEQ ID NO:242)

Translation:

LNERDCLNVDYFCGIPFVNGLCCSGNCVFCLHTPREVKLP (SEQ ID NO:243)

Toxin Sequence:

Asp-Cys-Leu-Asn-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Asn-Asn-Gly-Leu-Cys-Cys-
 Ser-Gly-Asn-Cys-Val-Phe-Cys-Leu-His-Thr-Xaa3-Arg-Xaa1-Val-Lys-Leu-Xaa3-[^] (SEQ ID
 NO:244)

Name: O6.4
Species: obscurus
Isolated: No
Cloned: Yes

DNA Sequence:

cgatccatctgtccatccatccattcattcattgccaaactgtaacaaatattcaagtctctcttctgtttgtctgacagATCGAAA
 CGGTGCCTTGTTCACGGTACACCTTGTGACTGGCTGACCATTGCGGGTATGGAGTGC
 TGCAGTAAAAAGTGCTTTATGATGTGCTGGTAACTGCCGTGATGCTCTTACTCC
 CCTC (SEQ ID NO:245)

Translation:

RSKRCLVYGTPCDWLTIAGMECCSKKCFMMCW (SEQ ID NO:246)

000221-25964760

Toxin Sequence:

5 Cys-Leu-Val-Xaa5-Gly-Thr-Xaa3-Cys-Asp-Xaa4-Leu-Thr-Ile-Ala-Gly-Met-Xaa1-Cys-Cys-Ser-
Lys-Lys-Cys-Phe-Met-Met-Cys-Xaa4-^ (SEQ ID NO:247)

Name: R6.4
Species: radiatus
 10 **Isolated:** No
Cloned: Yes

DNA Sequence:

15 ATTGAACCAGAGAGACTGCCATGAAGTTGGTGAATTTTGTGGCTTACCGTTAATAAA
 GAACGGGCTATGCTGCAGTCAGATTTGTTTAGGTGTCTGCGCAAAAGTGTTTAAAA
 CTGCCGTGATGTCTTCTACTCCCAT (SEQ ID NO:248)

Translation:

20 LNQRDCHEVGEFCGLPLIKNGLCCSQICLGVC AKVF (SEQ ID NO:249)

Toxin Sequence:

25 Asp-Cys-His-Xaa1-Val-Gly-Xaa1-Phe-Cys-Gly-Leu-Xaa3-Leu-Ile-Lys-Asn-Gly-Leu-Cys-Cys-
 Ser-Gln-Ile-Cys-Leu-Gly-Val-Cys-Ala-Lys-Val-Phe-^ (SEQ ID NO:250)

Name: R6.6
 30 **Species:** radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

35 ATTAGACAAGAAAGAGTGCCTGCCAATGGTGAATTTTGTGGCATATCGGTCTTTGG
 AAGCTACCTATGCTGCAGTGGCCGGTGTATTCTGCTGCATCTAGTTGAACTGCCG
 TGATGCTTCTACTCCCT (SEQ ID NO:251)

Translation:

40 LDKKECTANGEFCGISVFGSYLCCSGRCVFVCI (SEQ ID NO:252)

Toxin Sequence:

45 Xaa1-Cys-Thr-Ala-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Gly-Ser-Xaa5-Leu-Cys-Cys-
 Ser-Gly-Arg-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:253)

009221259600

Name: R6.7
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATTGGACAAGAAAGAGTGCCTACCAATGGTGAATTTTGTGGCATATCGGTCTTTGC
 AAGCTTCCTATGCTGCAGTGGCCTGTGTATTTCGTCTGCATCTAGCTGAACTGCCG
 TGATGTCTTCTCTCCCT (SEQ ID NO:254)

Translation:

LDKKECTTNGEFCGISVVFASFLCCSGLCVFVCI (SEQ ID NO:255)

Toxin Sequence:

Xaa1-Cys-Thr-Thr-Asn-Gly-Xaa1-Phe-Cys-Gly-Ile-Ser-Val-Phe-Ala-Ser-Phe-Leu-Cys-Cys-
 Ser-Gly-Leu-Cys-Val-Phe-Val-Cys-Ile-^ (SEQ ID NO:256)

Name: R6.8
Species: radiatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATTGGACAAGAGAAAATGCTTTCCCAAAAATCATTTTTGTGGCTTTGTGGTGATGCT
 GAACTACCTATGCTGCAGTGGCCGGTGTATATTCGTCTGCGTCTAGTTGAACTGCCG
 TGATGTCTTCTACTCCCAT (SEQ ID NO:257)

Translation:

LDKRKCFPKNHFCGFVVMLNYLCCSGRCIFVCV (SEQ ID NO:258)

Toxin Sequence:

Lys-Cys-Phe-Xaa3-Lys-Asn-His-Phe-Cys-Gly-Phe-Val-Val-Met-Leu-Asn-Xaa5-Leu-Cys-Cys-
 Ser-Gly-Arg-Cys-Ile-Phe-Val-Cys-Val-^ (SEQ ID NO:259)

Name: Rg6.5
Species: regius
Isolated: No

09749637.122800

Cloned: Yes

DNA Sequence:

5 TTGAACAAGAGAAGCTGCCTTCTAGACTGTTTTGTGGCTTCAATATAATTGGA
GCGTTTCTGTGCTGTAGTGGCTACTGCCTTGTGCTCTGCATGTAAAAGTCCCGTAT
GTCTTCTCCTCCCCTC (SEQ ID NO:260)

Translation:

10 LNKRSCLPLDWFCGFNIIGAFLCCSGYCLVVC (SEQ ID NO:261)

Toxin Sequence:

15 Ser-Cys-Leu-Xaa3-Leu-Asp-Xaa4-Phe-Cys-Gly-Phe-Asn-Ile-Ile-Gly-Ala-Phe-Leu-Cys-Cys-
Ser-Gly-Xaa5-Cys-Leu-Val-Val-Cys-Met-[^] (SEQ ID NO:262)

Name: De6.2
20 **Species:** delessertii
Isolated: No
Cloned: Yes

DNA Sequence:

25 ATGAAACTGACGTGCTGCTGATCGTTGCTGTGCTGGTCTTGGCAGCCTGTCAGTTC
ATCGTAGCTGGCGACTCGAGTGATGGCCAGGAGAATCCTGCTCTGAGGTCACCTAG
CGATTCTCTGGGAAAATGTCATCAATGAAGCGCTTCCAGACACGGCTGATGGTGG
GGCAATCTGCATCGAAAAGACCAAGCAAGAGGGACTGCATCCCCGGCGGCGAAAA
30 TTGTGATGTATTCCGACCATACCGGTGCTGCAGTGATATTCATATACTCCTTTG
CGCATGATAAAGCTGCCTTGATGTCTTCTCCTCCCCTC (SEQ ID NO:263)

Translation:

35 MKLTCLLIVAVLVLAACQFIVAGDSSDGQENPALRSPDSSGKMSSMKRFQTRLMVGQ
SASKRPSKRDICIPGGENCDVFRPYRCCSGYCILLCA (SEQ ID NO:264)

Toxin Sequence:

40 Asp-Cys-Ile-Xaa3-Gly-Gly-Xaa1-Asn-Cys-Asp-Val-Phe-Arg-Xaa3-Xaa5-Arg-Cys-Cys-Ser-
Gly-Xaa5-Cys-Ile-Leu-Leu-Leu-Cys-Ala-[^] (SEQ ID NO:265)

Name: Striat21
45 **Species:** striatus
Isolated: No
Cloned: Yes

09749637.122800

DNA Sequence:

GCTGGTTCGCCTGCAGGTACCGGTCCGGAATCCCGGGTCGACATCATCATCATCGA
 5 TCCATCTGTCCATCCATCTATTCAATTCATTTCGCTGCCAAACTGTATTAAATATT
 CAAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGATGGTGCAATTCCTAGTGGTGA
 ACTTTGTTTCCGCTCGGATACATAGGATGCTGCAGTGCCAAGTGCGCATTCGTCTG
 CTGTGAAAACCTGCCGTGATGTCTTCTCCTCCCATCTAGTAGTAGTAGGCGGCCGCTC
 10 TAGAGGATCCAAAGCTTACGTACGCGTGCATGCGACGTCATAGCTCTTCTATAGTGTC
 ACCTAAATTCAATTCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCCTGG
 CGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAG
 CGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTTGCAGCAGCTGAATGGCGAA
 TGGGACGCGCCCTGTAGCGGCGCATTAAACCGCGCGGGTGTGGGTGGGTACGCC
 CACGTGACCCGCTACACTTGCAGCGCCCTANCGCCCCGCTCCTTTCGCTTTCTTTCC
 15 CTTCTTTCTCGNACGTTTCGGCCGNTTTTCCCGTCAAGCTCTTAAATCGGGGGG
 CTTCCCTTTAAAGGGTTNCCGAATTANTGCTTACCAGNACCCTTGACCCCAAAAAA
 ACTTGGANTAAGGGGNGATGGNTCNCGTAANTGGGGGCCATCNCCTGAANAGA
 ACGGTTTTTNCNCCCTTTTGACNGTTGGNGTTCNCGGTTTTTAAAAAANGGGACC
 TTTTNTTCCAAAACTGGGAANANACCTAAACCCTATTTTGGGGCTATTTTTTGAN
 20 TTTNAAANGGGATTTTGCCCCATTTTNGGCCCTNTTGGGGTAAAAAAGAGCCGG
 TTTTAAAAAAATTTTACCCCAAATTTTAACAAAAATTTTTT (SEQ ID NO:266)

Translation:

25 LRWCIPSGELCFRSDHIGCCSGKCAVCL (SEQ ID NO:267)

Toxin Sequence:

30 Leu-Arg-Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-
 Ser-Gly-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:268)

Name: δStriatus 26
Species: striatus
 35 **Isolated:** No
Cloned: Yes

DNA Sequence:

40 TTGAGATGGTGCATTCCTAGTGGTGATCTTTGTTTCCGCTCGGATCACATAGGATGC
 TGCAGTGGCAAGTGCGCATTCGTCTGCTTGTA (SEQ ID NO:269)

Translation:

45 LRWCIPSGDLCFRSDHIGCCSGKCAVCL (SEQ ID NO:270)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-Lys-
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:271)

Name: δStriatus 106
Species: striatus
Isolated: No
Cloned: Yes

DNA Sequence:

TTGAGATGGTGCATTCTAGTGGTGATCTTTGTTTCCGCTCGGATCACATACAATGC
TGCAGTGGCAAGTGCGCATTCTGCTCTGTGTAA (SEQ ID NO:272)

Translation:

LRWCIPSGDLFRSDHIQCCSGKCAFVCL (SEQ ID NO:273)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-Lys-
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:274)

Name: O6.3
Species: obscurus
Isolated: No
Cloned: Yes

DNA Sequence:

cgatccatctgtccatccatccattcagtcgctgccaaactgtaacaaatattcaagtcttgccttctgtgtctgacagATTGAG
ATGGTGC GTTCCTAGCGGTGAAGTTTGTGCGCGCTATGAATTCGTGGGATGCTGCAG
TGGCAAGTGCTTCTCTGCTCTGCTCGTAAACTGTTGTGATGTCTTCTCCTCCCTC
(SEQ ID NO:275)

Translation:

VSDRLRWCVPSGEVCRRYEFVGGCSGKCFVCS (SEQ ID NO:276)

Toxin Sequence:

Leu-Arg-Xaa4-Cys-Val-Xaa3-Ser-Gly-Xaa1-Val-Cys-Arg-Arg-Xaa5-Xaa1-Phe-Val-Gly-Cys-
Cys-Ser-Gly-Lys-Cys-Phe-Phe-Val-Cys-Ser-^ (SEQ ID NO:277)

008221-2964260

Name: R6.3
Species: *radiatus*
Isolated: No
Cloned: Yes

DNA Sequence:

ctctctctctctctctgacaggtCGACTCGCTGCTTGCTGACGGAACGCTTGCCTTTTATGTA
 GGATCAGATGCTGCGGTACTTGCAGTTCAATCTTAAAGTCATGTGTGAGCTGATCCG
 GCGGTTGATCTTCCTCCCTCTGTGCTCCATCCTTTTCTGCCTGAGTCCTCCTTACCTG
 AGAGTGGTCATGAACCACTCATCACCTACTCCTCTGGAGGCTTCAGAGGAGCTACAT
 TGAAATAAAAGCCGATTGC (SEQ ID NO:278)

Translation:

RSTRCLPDGTSCLFSTRIRCCGTCSSILKSCVS (SEQ ID NO:279)

Toxin Sequence:

Cys-Leu-Xaa3-Asp-Gly-Thr-Ser-Cys-Leu-Phe-Ser-Arg-Ile-Arg-Cys-Cys-Gly-Thr-Cys-Ser-Ser-
 Ile-Leu-Lys-Ser-Cys-Val-Ser-^ (SEQ ID NO:280)

Name: G6.3
Species: *geographus*
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCTTGCACGGTGAATTTTCGCTTCATATTTTCTACTGTGCTCTTTGGCATCATCC
 AAAACATCACCAAGATGAACTGACGTGCATGATCGTTGCTGTGCTGTTCTTGA
 CCGCTGGACATTCGTACGGCTGTGCCTCACTCCAGCGATGTATTGGAGAATCTTT
 ATCTGAAGGCACTTACGAAACGAAAAACACGAAGCCTCTAAATTGAACGTGAGA
 GACGACGAGTGCGAACCTCCTGGAGATTTTGTGGCTTTTTAAAAATTGGGCCGCTT
 TGCTGCAGTGGCTGGTGTCTCCTCTGGTGCCTAAAACTGCCGTGATGTCTTCTATT
 CCCCTCTGTGTACCTGGCTTGATCTTTGATTGGCGCGTGCCCTTCAGTGGTTATGAA
 CCCCCCTGAGCCGACTCTCTGGGGGCCCTCGGGGGTTCAACATCCAATAAAGCGAC
 AACACAATCACAAGTAAAAAA (SEQ ID NO:281)

Translation:

MKLTCMMIVAVLFLTAWTFVTVAPHSSDVLENLYLKALHETENHEASKLNVDRDECEP
 PGDFCGFFKIGPPCCSGWCFWLCA (SEQ ID NO:282)

Toxin Sequence:

Asp-Asp-Xaa1-Cys-Xaa1-Xaa3-Xaa3-Gly-Asp-Phe-Cys-Gly-Phe-Phe-Lys-Ile-Gly-Xaa3-Xaa3-

Cys-Cys-Ser-Gly-Xaa4-Cys-Phe-Leu-Xaa4-Cys-Ala-[^] (SEQ ID NO:283)

Name: Tx6.8
Species: textile
Isolated: No
Cloned: Yes

DNA Sequence:

GCTGCAGGTCGACTCTAGAGGCGTTGGAGAATCTTTATCTGAAGGCACATCATGAA
 ATGAACAACCCCGAAGACTCTGAATTGAACAAGAGGTGCTATGATAGTGGGACAAG
 TTGTAACACTGGAAACCAATGCTGCAGTGGCTGGTGCATTTTCGTCTGCCTCTAAAA
 CTGCCGTGATGTCTTCTACTCCCCTCTGTGTACCTACCTGGCTTGATCTTTGATTGG
 CGCGTGCCCTTCACTGGTTATGAACCCCTCTGATCCGACTCTCTGGGGGCCCTCGGGG
 ATCCAACATCAAAATANAGCGACAGCACAAATCAC (SEQ ID NO:284)

Translation:

CRSTLEALENLYLKAHHEMNPNPEDSELNKRCDYSGTSCNTGNQCCSGWCIFVCL (SEQ
 ID NO:285)

Toxin Sequence:

Cys-Xaa5-Asp-Ser-Gly-Thr-Ser-Cys-Asn-Thr-Gly-Asn-Gln-Cys-Cys-Ser-Gly-Xaa4-Cys-Ile-
 Phe-Val-Cys-Leu-[^] (SEQ ID NO:286)

Name: Qc6.1
Species: quercinus
Isolated: No
Cloned: Yes

DNA Sequence:

GCTTCGTATTTCTCCGCTGTCTTCCTTGGCATCACCCAAAAACATCACCAAGATGAAA
 CTGACGTGCATGATGATCGTTGTCTGTCTGTTCTTGACCGCTGGACATTCGTCAAG
 GCTGTTGACTCCAAAAATGAACTGGAGaACAGAGGAGGATGGGGGCAGGCAGGAG
 GATGGGGGAAACTTTTCCGATGGCACGCGACGAAATGAAAAACAGCGAAGTCTCT
 AAATTGGACAATAAGAGAAAAGTGCCTGCAGCCGGTGAAGCTTGCCTAATACCTAT
 CATTGGAACGTATTTTGTGCAAAAGGCTACTGtCTTTTCGTCTGCATTAGTTAAACT
 GcTGTGATGcTtTCTACTCACCTCTGTGTACCTGGCTTGATCTTTGATTGGCGTGTGC
 CCTTCACTGGTTATGAgCTCGTCTGAtCCTACTCTCTGGAGACCTCTGTGGTCCAACAt
 CCaATAAAGCGGcATCCCAATC (SEQ ID NO:287)

Translation:

008221-42964760

MKLTCMMIVALLFLTAWTFVTAVDSKNELENRGGWGQAGGWGKLFPMARDEMKNSE
VSKLDNKRKCAAAGEACVIPITGNVFCCKGYCLFVCIS (SEQ ID NO:288)

5 **Toxin Sequence:**

Cys-Ala-Ala-Ala-Gly-Xaa1-Ala-Cys-Val-Ile-Xaa3-Ile-Ile-Gly-Asn-Val-Phe-Cys-Cys-Lys-Gly-
Xaa5-Cys-Leu-Phe-Val-Cys-Ile-Ser-^ (SEQ ID NO:289)

10 -----

Name: Lp6.5
Species: leopardus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGGATATTC
ATCACGGCTGATGACTCCACAAATGGACTGGAGAATCGTTTATAGGAAGGCACGTGA
CAACATGAAGAACGCCAAAGCCTCTACATTAGCCGAGAAGAAAGCGTGTGTGAAC
TTGGTGAGATTGTGCCACAGGCTTCTCTAGACGAGGAATGCTGCACTGGTTCAT
GCCATGTCTTCTGCGTACTATAGTTAAACTGCTGTGATGTCTTCTCTCCTCCGTG
CTACCTGGCTTGATCTTTGATTGGTGCCTGTCTTCAGTGTTGTGAAACCCTCTGAT
CCTACTCTCTGGACGCCTCTGAGGCCCAACATCCAAATAAAGCGACATCCTAATGCC
AAAAAAAAAAAA (SEQ ID NO:290)

Translation:

MKLTCVVIVAVLFLTAWIFITADDSTNGLENRFRKARDNMKNAKASTLAEKKACVELG
EICATGFFLDEECCTGSCHVFCVL (SEQ ID NO:291)

Toxin Sequence:

Ala-Cys-Val-Xaa1-Leu-Gly-Xaa1-Ile-Cys-Ala-Thr-Gly-Phe-Phe-Leu-Asp-Xaa1-Xaa1-Cys-Cys-
Thr-Gly-Ser-Cys-His-Val-Phe-Cys-Val-Leu-^ (SEQ ID NO:292)

Name: Mr6.4
Species: marmoreus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATT

09749637.122600

GCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTTTCGAAGGCACATCA
CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCCTAACACTGGTG
AATTATGTGATGTGGTTGAACAAAACCTGCTGCTATACCTATTGCTTTATTGTAGTCT
GCCTATAAAACTACCGTGATGTCTTCTACTCCCTCTGTGCTGCCTGGCTTGATCTTT
GATTGGCGCGTGCCCTTCACTGGTTATGACCCCTGATCCGACCTCTGGGG (SEQ
ID NO:293)

Translation:

MKLTCVVIVAVLFLTAWTFATADDPNRNGLNLFSAKHHMKNPASKLNKRCNPNTGEL
CDVVEQNCCYTYCFIVVCL (SEQ ID NO:294)

Toxin Sequence:

Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-
Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:295)

Name: Qc6.2
Species: quercinus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTATGGTGATCGTTGCTGTGCTATTCTTGACCGCCTCG
GCTGATGACTCCAGAAATGGATTGCGAGAATCGAAATGGAGAACGAAACGAAACG
AAATGAAGAACCTCGAAGCCTCTAAATTGAACAGGAGAGACGGCGATTGCGTTGAT
GGTGGTGAATTTTGTGGCTTCCGAAAATTGGAGGGCCATGCTGTAGTGGCTGGTGC
TTTTTCGTCTGCTTATAAACTGCCATGATGTCTTCTACCCCCCTCTGTGCTACCTGA
CTTGATCTTTGATTGGCGTGTGCCCTTCACTGGTTATGAACCCCTCTGATCCGACTCT
CTGGAGGCCTCGGGGGTCCAACATCCAAATAAAGCGACAGCAAAAAAAAAAAAAA
AAAAAA (SEQ ID NO:296)

Translation:

MKLTCMVIVAVLFLTASADDSRNGFENRNGERNENEMKNLEASKLNRRDGDGDCVDGGE
FCGFPKIGGPCCSGWCFVCL (SEQ ID NO:297)

Toxin Sequence:

Asp-Gly-Asp-Cys-Val-Asp-Gly-Gly-Xaa1-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-
Cys-Ser-Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-^ (SEQ ID NO:298)

09749637.1.22800

Name: Qc6.3
Species: quercinus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGCTATTCTTGACCGCCTTG
 GCTGATGACTCCAGAAATGGATTGGAGAATCGAAATGAACAAGAACGAAACGAAA
 ACGAAATGAGGGACCGCCGGGACTGCCAAGATAGTGGTGTAGTTTGTGGCTTTCCG
 AAACCTGAACCACTGCTGCAGTGGCTGGTGCCTTTTCGTCTGCGCCTAAACTGC
 CGTGATGTCAAATAAAGCGACAGACAATNAAAAAAAAAAAAAAAAAAAAA (SEQ ID
 NO:299)

Translation:

MKLTCVVIVAVLFLTLALADDSRNGLENRNEQERNENEMRDRDCQDSGVVCGFPKPEP
 HCCSGWCLFVCA (SEQ ID NO:300)

Toxin Sequence:

Asp-Cys-Gln-Asp-Ser-Gly-Val-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Xaa1-Xaa3-His-Cys-Cys-
 Ser-Gly-Xaa4-Cys-Leu-Phe-Val-Cys-Ala-^ (SEQ ID NO:301)

Name: Ar6.5
Species: arenatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTGTTCCTTGACCGCCTGG
 ACATTGCTCACGGCTGACTCCATACGTGCACTGGAGGATTTTTTGCGAAGGCACGT
 GACGAAATGGAACAGCGGAGCTTCTCCATTGAACGAGAGAGACTGCCGACCTGT
 AGGTCAATATTGTGCATACCGTATAAGCACAACTGGCGATGCTGCAGTCAGCTTTG
 TGCAATTATCTGTGTTTCTAACCCCTCTGATCTACTCTCTGAAGACCTCCGGGATT
 CAACATCCAAATAAAGCGACATCCCGATNAAAAAAAAANGAAAAAAAAAAAAAAAAA
 (SEQ ID NO:302)

Translation:

MKLTCVVIVAVLFLTAWTFVTADSIRALEDFFAKARDEMENS GASPLNERDCRPVGY
 CGIPYKHNWRCCSQLCAIICVS (SEQ ID NO:303)

Toxin Sequence:

008221-122800

Asp-Cys-Arg-Xaa3-Val-Gly-Gln-Xaa5-Cys-Gly-Ile-Xaa3-Xaa5-Lys-His-Asn-Xaa4-Arg-Cys-
Cys-Ser-Gln-Leu-Cys-Ala-Ile-Ile-Cys-Val-Ser-^ (SEQ ID NO:304)

5 -----

Name: Ar6.11
Species: arenatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGTTGTGCTGTTCTTGACCGCCTGG
ACATTCGTC AAGGCTGATGACTCCATAAATGGATTGGAGAATCTTTTCCGAAGGCA
CGTCACGAAATGAAGAACCCCGAAGCCTCTAAATTGGAACGAGAGGTGCCTTGAAAA
GGGTGTACTTTGTGATCCGAGTGCTGGAAACTGCTGTAGTGGCGAATGCGTTTTAGT
CTGCCTCTAAAACCTACCGTGATGCTCTTCTACTCCCATCTGTGCTACCCCTCGAG (SEQ
ID NO:305)

Translation:

MKLTCVVIVVVLFLTAWTFVKADDSINGLENLFPKARHEMKNPEASKLNERCLEKGVL
CDPSAGNCCSGECVLVCL (SEQ ID NO:306)

Toxin Sequence:

Cys-Leu-Xaa1-Lys-Gly-Val-Leu-Cys-Asp-Xaa3-Ser-Ala-Gly-Asn-Cys-Cys-Ser-Gly-Xaa1-Cys-
Val-Leu-Val-Cys-Leu-^ (SEQ ID NO:307)

Name: Ar6.12
Species: arenatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCATGGTGATCGTTACTGTGTTGTTCTTGACCGCCTGG
ACATTCGTCACGGCTGATGACTCCAGAAATGAATTGGAGAATCTTTTCTGAAGGCA
TATCACGAAATGAACCTCCGAAGCCTCTAAATTGGACAAGAAAGAGTGCGTTGCTGG
TAGTCACITTTGTGGTTTTCCGAAAATTGGAGGGCCATGCTGCAGTGGCTGGTGCTT
TTTCGTCTGCTTGTAACCTGCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCG
AG (SEQ ID NO:308)

Translation:

00821-122800

MKLTCMVIVTVLFLTAWTFVTADDSRNELENLFLKAYHEMNSEASKL DKKECVAGSHF
CGFPKIGGPCCSGWCFFVCL (SEQ ID NO:309)

5 **Toxin Sequence:**

Xaa1-Cys-Val-Ala-Gly-Ser-His-Phe-Cys-Gly-Phe-Xaa3-Lys-Ile-Gly-Gly-Xaa3-Cys-Cys-Ser-
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Leu-[^] (SEQ ID NO:310)

10 -----

Name: Ts6.2
Species: tessulatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGATGTTCTTGACCGCCTGG
ACATTTCATCAGCGGTGATGACTCCATAAATGGACTGGAGGATAGAGGCATATGGGG
GGAACCTTTGTCTGAAGGCACGTGACGAAATGAACCCCGAAGTCTCTAAACGGGATT
GCTGGCCTCAATATTGGTTTGTGTGCCTACAGAGGGGATGCTGCCAGGGACTACTT
GCTTCTTCTTTGTCTTTAGTGATCTCTTCGACTCCCTTCTGTGCTACCTGGCTTGACC
TTTGATTGGCGCGTGCCCTTCACTGGTTATAAACCCCTCTGTTCCTCTCTCTGGACG
CTTCGGGGTGTCCAGCATCCAAATAAAGCGACGTCCCCAAAAAAAAAAAAAAAAAAAA
AA (SEQ ID NO:311)

Translation:

MKLTCVVIVAVMFLTAWTFITADDSINGLED RGIWGEPLSKARDEMNPVSKRDCWPQ
YWFCGLQRGCCPGTTCCFLCF (SEQ ID NO:312)

Toxin Sequence:

Asp-Cys-Xaa4-Xaa3-Gln-Xaa5-Xaa4-Phe-Cys-Gly-Leu-Gln-Arg-Gly-Cys-Cys-Xaa3-Gly-Thr-
Thr-Cys-Phe-Phe-Leu-Cys-Phe-[^] (SEQ ID NO:313)

Name: Ts6.4
Species: tessulatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGGTCGTTGCTGTGCTGTTCTTGAACGCCTGG

08221" 4E6H460
20
25
30

ACATTGCCACGGCTGTTGACTCCAAACATGCACTGGCGAACTTTTATGAAGGCA
 CGTGACGAAATGTATAACCCCGATGCCACTAAATTGGACGATAAGAGATGGTGCGC
 TTTAGATGGTGAACTTTGTATCATACCCGGTCATTGGGTCCATATTTTGTGCCATGGC
 ATATGTATGATCTACTGCGTCTAGTTGAAGTCCGCTGATGTCTTCTACTCCCCTCTGT
 5 GCTACCCCTGGTTTGATCTTTGATTGCCCTGTGCCCTTCACTGATTATGAATCCCTCT
 GATCCTACTCTCTGAAGACCTCTTGGGGTCCAAACATCCAAATAAAGCGACATCCCAA
 AAAAAAAAAAAAAAAAAA (SEQ ID NO:314)

Translation:

10 MKLTCVVVVAVLFLNAWTFATAVDSKHALAKLFMKARDEMYNPDATKLDDKRWCA
 LDGELCIIPVIGSIFCCHGICMIYCV (SEQ ID NO:315)

Toxin Sequence:

15 Xaa4-Cys-Ala-Leu-Asp-Gly-Xaa1-Leu-Cys-Ile-Ile-Xaa3-Val-Ile-Gly-Ser-Ile-Phe-Cys-Cys-His-
 Gly-Ile-Cys-Met-Ile-Xaa5-Cys-Val-^ (SEQ ID NO:316)

20 -----
Name: Im6.1
Species: imperialis
Isolated: No
Cloned: Yes

DNA Sequence:

25 GGATCCATGAAACTGACGTGCGTGGTGTTTCGTTGCTGTGCCGTTCTTGACCGCCTCG
 GTATTCATCACGGCTGATGACTCCAGAAATGGAATCGAGAATCTTCCTCGGATGAG
 30 ACGTCACGAAATGAAGAACCCCAAAGCCTCTAAGTTGAACAAGAGACAGTGCCGTG
 TAGAAGGTGAAATTTGTGGCATGCTGTTGAAGCACAATGCTGCGATGGCTGGTGCT
 TTTTCGTCTGCATGTAAAACTGCCGTGATGTCCTTCTACTCTCCTCTGTGCTACCTGCC
 CTGATCTTTGATTGGCTCGCGCCCTTCATTGGTTATGAACCCCTCTGATCCTACTCTC
 35 TGGAGGCCTCAGGGGTCCAGCATCTAAATAAAGCGACATCAATCAAAAAAAAAA
 AAAAAAAAAA (SEQ ID NO:317)

Translation:

40 MKLTCVVVFAVPFLTASVFITADDSRNGIENLPRMRHEMKNPKASKLNRQCRVEGEI
 CGMLFEAQCCDGWCFVCM (SEQ ID NO:318)

Toxin Sequence:

45 Xaa2-Cys-Arg-Val-Xaa1-Gly-Xaa1-Ile-Cys-Gly-Met-Leu-Phe-Xaa1-Ala-Gln-Cys-Cys-Asp-
 Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Met-^ (SEQ ID NO:319)

008221' 25964760

Name: Ca6.5
Species: characteristic
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG
 ACATTCGTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTTCCGAAGGCA
 CGTCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCGTTGACCC
 TGGTGAATTTTGTGGTCCGGGATTTGGAGATTGCTGCACTGGCTTCTGCCTTTTAGTC
 TGCATCTAAAACTGCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCGAG (SEQ
 ID NO:320)

Translation:

MKLTCVVIVAVLFLTAWFTVTTADDSRNGLENLFPKARHEMKNPEASKLNKRCVDPGEF
 CGPGFGDCCTGFCLLVCI (SEQ ID NO:321)

Toxin Sequence:

Cys-Val-Asp-Xaa3-Gly-Xaa1-Phe-Cys-Gly-Xaa3-Gly-Phe-Gly-Asp-Cys-Cys-Thr-Gly-Phe-Cys-
 Leu-Leu-Val-Cys-Ile-^ (SEQ ID NO:322)

Name: Mf6.2
Species: miliaris
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCGTTGCTGTGTTGTTCTTGACCGCCTGG
 ACATTCGTCATGGCTGATGACTCCAGAAATGATTTGGAGAATCTTTTCTGAAGGCA
 CGTCATGAAATGAAGAACCCCGAAGCTTCTAAATTGAACAAGAGATGCCTTCCAAA
 TGGTGTACTTTTGTGATCTGGGATCTCCACCATACTGCTGCACTGGCTGGTGCGCGAT
 CGTCGTCTGCATCTAAAACTGTCGTCATGTCTTCTACTCCCATCTGTGCTACCCCTCG
 AG (SEQ ID NO:323)

Translation:

MKLTCVVIVAVLFLTAWFTVMADDSRNDLENLFLKARHEMKNPEASKLNKRCLPNGV
 LCDLGSPPYCCSGWCAIVVCI (SEQ ID NO:324)

008221-23964760

Toxin Sequence:

Cys-Leu-Xaa3-Asn-Gly-Val-Leu-Cys-Asp-Leu-Gly-Ser-Xaa3-Xaa3-Xaa5-Cys-Cys-Ser-Gly-Xaa4-Cys-Ala-Ile-Val-Val-Cys-Ile-^ (SEQ ID NO:325)

Name: Ak6.1
Species: atlanticus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGCGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG
ACATTTCGTACGGCTGATGACTCCATAAATGGGTGGAGAATCTTTTCCGAAGGCA
CGTCACGAAATGAGGAAACCCGAAGCCTCTAGATCGAGAGGGAGGTGCCGTCTCTCG
TGGTATGTTCTGTGGCTTTCCGAAACCTGGACCATACTGCTGCAATGGCTGGTGCTT
TTTCGTCTGCATCTAAAACTGCCGTGATGTGTTCTACTCCCATCTGTGCTACCCCTCG
AG (SEQ ID NO:326)

Translation:

MKLTCVVIVAVLFLTAWTFVTADDSINGLENLFPKARHEMRKPEASRSRGRCPRGMF
CGFPKPGPYCCNGWCFFVCI (SEQ ID NO:327)

Toxin Sequence:

Cys-Arg-Xaa3-Arg-Gly-Met-Phe-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Asn-Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ile-^ (SEQ ID NO:328)

Name: Lv6.1
Species: lividus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGCGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG
ACATTTCGCCACGGCTGATGACCCAGAAATGGATTGGAGAATCTTTTTCGAAGGCA
CATCACGAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGGTGCCCTAACAC
TGGTGAATTATGTGATGTGGTTGAACAAAACCTGCTGCTATACCTATTGCTTTATTGT
AGTCTGCCATATAAACTACCGTATGCTCTTCTACTCCCATCTGTGCTACCCCTCGAG
(SEQ ID NO:329)

Translation:

MKLTCVVIVAVLFLTAWTFATADDPNGLNLFKSAHHEMKNPEASKLNKRCNPNTGEL
CDVVEQNCCYTYCFIVVCL (SEQ ID NO:330)

Toxin Sequence:

Cys-Xaa3-Asn-Thr-Gly-Xaa1-Leu-Cys-Asp-Val-Val-Xaa1-Gln-Asn-Cys-Cys-Xaa5-Thr-Xaa5-
Cys-Phe-Ile-Val-Val-Cys-Leu-^ (SEQ ID NO:331)

Name: Pu6.3
Species: pulicarius
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCATGGTGATCGTTGCTGTGCTGTTCTTGACCGCCTGG
ACATTCGTCAAGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTTCCGAAGGC
ACGTCACGAAATGAAGAACTCCAAAGCCTCTAAATTAACAAGAGGTGCGTTGAAG
ATGGTGATTTTTGTGGTCCGGGATATGAAGAGTGTCTGCAGTGGCTTCTGCCTTTACG
TCTGCATCTAAACTGCCGTGATGTCTTCTACTCCCATCTGTGCTACCCCTCGAG
(SEQ ID NO:332)

Translation:

MKLTCMVIVAVLFLTAWTFVKADDSRNGLENLFPKARHEMKNKASKLNKRCVEDGD
FCGPGYEECCSGFCLYVCI (SEQ ID NO:333)

Toxin Sequence:

Cys-Val-Xaa1-Asp-Gly-Asp-Phe-Cys-Gly-Xaa3-Gly-Xaa5-Xaa1-Xaa1-Cys-Cys-Ser-Gly-Phe-
Cys-Leu-Xaa5-Val-Cys-Ile-^ (SEQ ID NO:334)

Name: Ge6.1
Species: generalis
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCGTTGCTGTGCTATTCTTGACCGCCTGG
ACATTCGTACGGCTGATGACACCAGATATAAACTGGAGAATCCTTTTCTGAAGGC

ACGCAACGAACTGCAGAAACACGAAGCCTCTCAACTGAACGAGAGAGGCTGCCTTG
 ACCCAGGTTACTTCTGTGGGACGCCGTTTCTTGGAGCATACTGCTGCGGTGGCATT
 GCCTTATTGTCTGCATAGAAACGTAAAGGCTTGATGTCTTCTACTCCCATCTGTGCT
 ACCCTCGAG (SEQ ID NO:335)

Translation:

MKLTCCVVIVAVLFLTAWTFVTADDTRYKLENPFLKARNELQKHEASQLNERGCLDPGY
 FCGTPFLGAYCCGGICLIVCIET (SEQ ID NO:336)

Toxin Sequence:

Gly-Cys-Leu-Asp-Xaa3-Gly-Xaa5-Phe-Cys-Gly-Thr-Xaa3-Phe-Leu-Gly-Ala-Xaa5-Cys-Cys-
 Gly-Gly-Ile-Cys-Leu-Ile-Val-Cys-Ile-Xaa1-Thr-^ (SEQ ID NO:337)

Name: Ep6.1
Species: episcopatus
Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGCGTATCGTTGCTGTGCTGTCTTGGACCGCCTGG
 ACATTTGCCACGGCTGATGACCCCAGAAATGGATTGGGGAATCTTTTTCGAATGTA
 CATCACGAAATGAAGAACCTCGAAGACTCTAAATTGGACAAGAAGTGCTTGGGTT
 TGGTGAAGCTTGTCTTATGCTTTATTCAGACTGCTGCAGCTATTGCGTTGCTCTTGTC
 TGCCTATAAACTACCGTGACGTCTTCTACTCCCCCTGTGTGCTACCTGGCTTGATCTT
 TGATTGGCGTGTGCGCTTCACTGGTTATGAACCCCTCTGATCCTACTCTCTGAAGAC
 CTCTGGGTCCAAACATCCAAATAAAGCGACATCACAAAAAAAAAAAAAAAAAAAAAA
 AA (SEQ ID NO:338)

Translation:

MKLTCCVVIVAVLFLTAWTFATADDPRNGLGNLFSNVHHEMKNLEDSKLDKKCLGFGE
 ACLMLYSDCSYCVLALVCL (SEQ ID NO:339)

Toxin Sequence:

Cys-Leu-Gly-Phe-Gly-Xaa1-Ala-Cys-Leu-Met-Leu-Xaa5-Ser-Asp-Cys-Cys-Ser-Xaa5-Cys-Val-
 Ala-Leu-Val-Cys-Leu-^ (SEQ ID NO:340)

Name: Ep6.2
Species: episcopatus

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Isolated: No
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCATTGCTGTGCTGTTCTTGACCGCCTGG
ACATTCGTCATGGCTGATGACCCAGAGATGAACCGGAGGCACGTGACGAAATGAA
CCCCGCAGCCTCTAAATTGAACGAGAGAGGCTGCCTTGCACTTGATTATTTTGGCGG
CATACCGTTTGTGAGCAACGGGCTATGCTGCAGTGGCAATTGTGTTTTGTCTGCAC
ACCCCAAGGGAAGTAAAACTGCCGTGACGTCTTCTACTCCCTCTGTGTACCTGGC
TTGATCTTTGATTGGCGTGTGCACTTCACTGGTTATGAACCCCTCTGATCCTACTCTC
TGAAAGACCTCTGGGGTCCAACATCCAATAAAGCGACATCCCAAAAAAAAAAAAAA
AAAAAA (SEQ ID NO:341)

Translation:

MKLTCVVIHAVLFLTAWTFVMADDPREDEPEARDEMNPAAASKLNERGCLAVDYFCGIPF
VSNGLCCSGNCVVFVCTPQ GK (SEQ ID NO:342)

Toxin Sequence:

Gly-Cys-Leu-Ala-Val-Asp-Xaa5-Phe-Cys-Gly-Ile-Xaa3-Phe-Val-Ser-Asn-Gly-Leu-Cys-Cys-
Ser-Gly-Asn-Cys-Val-Phe-Val-Cys-Thr-Xaa3-Gln-# (SEQ ID NO:343)

Name: Ac6.1
Species: achatinus
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCTCTGTCCTCCATCTATTATTTCGCTGCCAACTGTGTTAAATATTCAAGT
CTCTCTTTCTGTTTGTGTCTAACAGGTTGAGATGGTGCAATTCCTAGAGGTGATCTTTG
TTCCCTCGGATCGCATACAATGCTGCAGTGGCAAGTGCACATTCGTCTGCATGTA
AAACTGCCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:344)

Translation:

LRWCIPRGDLCPSPDRIQCSCGKCTFVCM (SEQ ID NO:345)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Arg-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-Arg-Ile-Gln-Cys-Cys-Ser-Gly-
Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:346)

Name: Ac6.2
Species: achatinus
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCTCTGTCCTCCTCCTTCATTCATTGCTGCCAAACTGTATTAAATATTCGAAT
 CTCTCTTTCTGTTGTGTCTGACAGATTGAGAGGGTGCGTTCTAGTGGTGAAATTTG
 TTACTTCATGGATCACATAGGATGCTGCAGTGGCAAGTGCACATTCGTCCTGCATGTA
 AAACTGCCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:347)

Translation:

LRGCVPSGEICYFMDHIGCCSGKCTFVCM (SEQ ID NO:348)

Toxin Sequence:

Gly-Cys-Val-Xaa3-Ser-Gly-Xaa1-Ile-Cys-Xaa5-Phe-Met-Asp-His-Ile-Gly-Cys-Cys-Ser-Gly-
 Lys-Cys-Thr-Phe-Val-Cys-Met-^ (SEQ ID NO:349)

Name: Bu6.7
Species: bullatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGATGACTCCACATATGGATTGAAGAATCTTTTGCCGAACCGGACGTCAT
 GAAATGATGAACCCGAAGCCCTAAATTGAACAAGAAAGATGAATGCTCTGCTCC
 TGGTGCAATTTTGTCTCATCAGGCCAGGACTCTGCTGCAGCGAGTTCTGCTTCTTTGCG
 GTTTTTAGTGACGGTTGATGTCTTCTACTCCCCTC (SEQ ID NO:350)

Translation:

MKLTCVMIVTVLFLTAWTFVTADDSTYGLKNLLPNGRHEMMNPEAPKLNKKDECSAP
 GAFCLIRPGLCCSEFCFFACF (SEQ ID NO:351)

Toxin Sequence:

Asp-Xaa1-Cys-Ser-Ala-Xaa3-Gly-Ala-Phe-Cys-Leu-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
 Phe-Cys-Phe-Phe-Ala-Cys-Phe-^ (SEQ ID NO:352)

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Name: Bu6.8
Species: bullatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCGTGATGATCGTTACTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGATGACTCCAGAGACGCTCCGGATAGTGACAGAAAGGATGGGAGAAACT
 TTCTCGGAGGCACGTGACGAAATGAAGAACCGCAAAGACTTTGAATTGAGAGGGT
 GCCTTCCTAGGTGGGAATTTGTCCCATCTTTAAAAAAACGATTGCTGCAGTGGCA
 TATGCATAAGCATCTGCTTGTAACCTCCGTGATGTCTTCTTCCCATC (SEQ ID
 NO:353)

Translation:

MKLTCVMIVTVLFLTAWTFVTADDSRDAPDSAEGWEKLFSEARDEMKNRKDFELRGC
 LPRWEFCPIFKKNDCCSGICISICL (SEQ ID NO:354)

Toxin Sequence:

Gly-Cys-Leu-Xaa3-Arg-Xaa4-Xaa1-Phe-Cys-Xaa3-Ile-Phe-Lys-Lys-Asn-Asp-Cys-Cys-Ser-
 Gly-Ile-Cys-Ile-Ser-Ile-Cys-Leu-^ (SEQ ID NO:355)

Name: Sx6.4
Species: striolatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATTGTTGCTGTGCTGTTCTTGACCGCCTGGATATTT
 GTAATGGCTGATGACTCCAGAAATGGATTGGAGAATCTTCTCAGACTACACGTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATTGAACCAGACAGACTGCCTTGCTAAAG
 ACGCTTTCTGTGCTGGCCGATACTGGACCACTGTGCTGCAGTCGCTTGTGCTTAT
 ACGTCTGCATGtaaAACTGCCGTGATGTCTTCTACTCCCCTC (SEQ ID NO:356)

Translation:

MKLTCMMIVAVLFLTAWIFVMADDSRNGI ENLPQTTRHEMKNPEASKLNQTDCLAKD
 AFCAWPILGPLCCSRLCLYVCM (SEQ ID NO:357)

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Toxin Sequence:

Asp-Cys-Leu-Ala-Lys-Asp-Ala-Phe-Cys-Ala-Xaa4-Xaa3-Ile-Leu-Gly-Xaa3-Leu-Cys-Cys-Ser-Arg-Leu-Cys-Leu-Xaa5-Val-Cys-Met-^ (SEQ ID NO:358)

Name: Cn6.9
Species: consors
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGTATTCTA
CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTT
CTGTGCTTAAACATTTTCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:359)

Translation:

MKLTCMMIVAVLFLTAWTFVTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST
GTFCGNGGLCCSNLCLFFVCLTFS (SEQ ID NO:360)

Toxin Sequence:

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:361)

Name: Cn6.10
Species: consors
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCCTGATGATCGTTGCTGTGCTGTTCTTGACCACCTGGACATTC
GTCACGGCTGATGACTCCAGATATGGATTGAAGAATCTTTTCCGAAGGCACGTCA
GAAATGAAGAACCCCTGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTATAATGC
TGGTACATTTTGTGGCATCCGTCCAGGACTCTGCTGCAGCGAGTTTGTCTTTTATGG
TGCATAACATTTGTTGATTCTGGCTAACAGTGTGCGTTGGTTGATGTCTTCTACTCCC
CTC (SEQ ID NO:362)

Translation:

MKLTCLMIVAVLFLTWTFTVTTADDSRYGLKNLFPKARHEMKNPEASKLNKRDGCYNA
GTFCGIRPGLCCSEFCFLWCITFVDSG (SEQ ID NO:363)

5 **Toxin Sequence:**

Asp-Gly-Cys-Xaa5-Asn-Ala-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Val-Asp-Ser-# (SEQ ID NO:364)

10 -----

Name: Cr6.6
Species: circumciscus
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGCCAAACTGTATTAATATTC
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCCGATCACATAACAATGCTGCAATGCCAAGTGCGCATTCGTCTGCTT
GTAAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:365)

Translation:

NRLSRCIPSGDLCPSPDHIQCCNAKCAFVCL (SEQ ID NO:366)

Toxin Sequence:

Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-
Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:367)

Name: Cr6.5
Species: circumciscus
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGTCAAACGTATTAATATTC
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCTAGTGGTGATC
TTTGTTCCTCCGATCACATAACAATGCTGCAAGTGCGCATTCGTCTGCTT
GTAAAACTGCCGTGATGTCTTCTACTCCCTC (SEQ ID NO:368)

Translation:

NRLSWCIPSGDLCFPSDHIQCCSAKCAVCL (SEQ ID NO:369)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:370)

Name: Cr6.5A
Species: circumcised
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGTCAAACGTATTAAATATTC
AAGTCTCTCTTTCTGTTGTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCCCTCGGATCACATAAATGCTGCAGTGCCAAGTGCATTCGCTGCTT
GTAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:371)

Translation:

NRLSRCIPSGDLCFPSDHIQCCSAKCAVCL (SEQ ID NO:372)

Toxin Sequence:

Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:373)

Name: Cr6.6A
Species: circumcised
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGCCAAACGTATTAAATATTC
AAGTCTCTCTTTCTGTTGTGTCTAACAGATTGAGTAGGTGCATTCTAGTGGTGATC
TTTGTTCCTCCCTCGGATCACATAAATGCTGCAATGCCAGTGCATTCGCTGCTT
GTAAACTGCCGTGATGTCTTCTCTCCCTC (SEQ ID NO:374)

Translation:

NRLSRCIPSGDLCFPSDHIQCCNAECAVCL (SEQ ID NO:375)

Toxin Sequence:

- 5 Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Xaa1-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:376)

10 **Name:** Cr6.5B
Species: circumcised
Isolated: No
Cloned: Yes

15 **DNA Sequence:**

CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGTCAAACGTATTAAATATTC
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTTGGTGCATTCCTAGTGGTGATC
TTTGTTCCTCCCTCGGATCACATACGATGCTGCAGTGCCAAGTGCGCATTCGCTCGCT
20 GTAAAACTGCCGTGATGTCTTCTCTTCCCATC (SEQ ID NO:377)

Translation:

NRLSWCIPSGDLCFPSDHIRCCSAKCAVCL (SEQ ID NO:378)

25 **Toxin Sequence:**

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Arg-Cys-Cys-Ser-Ala-
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:379)

30 **Name:** Cr6.6B
Species: circumcised
35 **Isolated:** No
Cloned: Yes

DNA Sequence:

40 CGATCCATCTGTCCATCCATCTATTCAATTCATTCGCTGCCAAACGTATTAAATATTC
AAGTCTCTCTTTCTGTTTGTGTCTAACAGATTGAGTAGGTGCATTCCTAGTGGTGATC
TTTGTTCCTCCCTCGGATCACATACAATGCTGCAATGCCAAGTGCGCATTCGCTGCT
GTAAAACTGCCGTGATGTCTTCTTCCCTC (SEQ ID NO:380)

45 **Translation:**

NRLSRCIPSGDLCFPSDHIQCCNAKCAACL (SEQ ID NO:381)

09749637-122800

Toxin Sequence:

Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-Lys-
Cys-Ala-Phe-Ala-Cys-Leu-^ (SEQ ID NO:382)

Name: Cr6.6C
Species: circumcised
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCATCTGTCCATCCATCTATTCAATTCATTGCTGCCAAACTGTATTAAATATTC
AAGTCTCTCTTTCTGTTGTCTAACAGATTGAGTTGGTGCAATCCTAGTGGTGATC
TTGTTTCCCTCGGATCACATACAATGCTGCAATGCCAAGTGGCATTCTGCTGCTT
GTAAAACTGCCGTGATGTCTTCTACTCCCCTC (SEQ ID NO:383)

Translation:

NRLSWCIPSGDLCFPSDHIQCCNAKCAFVCL (SEQ ID NO:384)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Asn-Ala-
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:385)

Name: Cr6.7
Species: circumcised
Isolated: No
Cloned: Yes

DNA Sequence:

CGATCCTCTGTCCTCCTCTATTATTATTCGCTGCCAACTGTATTAAATATTCAAGTCT
CTCTTTCTGTTGTGTCTAACAGATTGAGTTGGTGCAATCCTACTGGTGATCTTTGTT
TCCCTCGGATCACATACAATGCTGCAGTGGCAAGTGCACATTCGCTCTGCATGTAAA
ACTGCCGTGATGTCTTCTCTCCCCTC (SEQ ID NO:386)

Translation:

NRLSWCIPTGDLCFPSDHIQCCSGKCTFVCM (SEQ ID NO:387)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Thr-Gly-Asp-Leu-Cys-Phe-Xaa3-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Gly-Lys-Cys-Thr-Phe-Val-Cys-Met-[^] (SEQ ID NO:388)

Name: Mn6.3
Species: monachus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA
 CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGTCTATTCTA
 CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTGCAGCAACCTTTGCTTATTTTT
 CGTGTGCTTAACATTTTCGTGATGTCTTCTCCTCCCCTC (SEQ ID NO:389)

Translation:

MKLTCMMIVAVLFLTAWFVTTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST
 GTFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:390)

Toxin Sequence:

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-[^] (SEQ ID NO:391)

Name: Sm6.5
Species: stercusmuscarum
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATGATGATCGTTGCTGTGCTGTTCTTGACCGCCTGGACATTC
 GTCACAGCTGATGACTCCATAAATGGACCGGAGAATAGACGAATATGGGAGAAACT
 TTTGTTGAAGGCACGTGACGAAATGAAGAACCCCGAAGCCTCTCAATTGAGATGGT
 GCATTCCTAGTGGTGAACCTTTGTTCCGCTCGGATCACATACAATGCTGCAGTGCCA
 AGTGCGCATTCGCTGCTTGTA AAACTACCGTGATGTCTTCTCCTCCCCTC (SEQ ID
 NO:392)

Translation:

MKLTCMMIVAVLFLTAWTFVTADDSINGPENRRIWEKLLLKARDEMKNPEASQLRWCI
PSGELCFRSDHIQCCSAKCAFVCL (SEQ ID NO:393)

Toxin Sequence:

Xaa4-Cys-Ile-Xaa3-Ser-Gly-Xaa1-Leu-Cys-Phe-Arg-Ser-Asp-His-Ile-Gln-Cys-Cys-Ser-Ala-
Lys-Cys-Ala-Phe-Val-Cys-Leu-^ (SEQ ID NO:394)

Name: Sm6.6
Species: stercusmuscarum
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTGTGATGATCGTTGCTGTGCTGTTCTTGATCGCCTGGACATTC
GTCACGGCTGATGACTCCAGAAATGGATTGAAGAATCTTTTCCGAAGGCACGTCAT
GAAATGAAGAACCCCGAAGCCTCTAAATTGAACAAGAGAGATGGGTGCTCTAGTGG
TGGTACATTTTGTGGCATCCGTCAGGACTCTGCTGCAGCGAGTTTGTCTTCTTTGG
TGCATAACATTTATTGATTGATGTCTTCTATTCCCCTC (SEQ ID NO:395)

Translation:

MKLTCVMIVAVLFLIAWTFVTADDSRNLKLNLFKARHEMKNPEASKLNKRDGCSSGG
TFCGIRPGLCCSEFCFLWCITFID (SEQ ID NO:396)

Toxin Sequence:

Asp-Gly-Cys-Ser-Ser-Gly-Gly-Thr-Phe-Cys-Gly-Ile-Arg-Xaa3-Gly-Leu-Cys-Cys-Ser-Xaa1-
Phe-Cys-Phe-Leu-Xaa4-Cys-Ile-Thr-Phe-Ile-Asp-^ (SEQ ID NO:397)

Name: Sx6.5
Species: striolatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGCATAATGACCGTTGCTGTGCTGTTCTTGACCGCTTGGACATTC
GTCACGGCTGATGACTCCAGAAATGTCATTGAGAATCTTCTTCTGAAGACACGTCA
CGAAGTGGAAAAACCCCAAGCCTCTAGGTCGGGCGGTAGGTGCCGCTCTGGTGGTA
CGGTTTGTGGCTTTCGAAACCTGGACCATACTGCTGCAGTGGCTGGTGCTTTTTTGT

CTGCGCCTAAACCTGCCGTGATGTCTTCTCCTCCCATC (SEQ ID NO:398)

Translation:

- 5 MKLTCIMTVAVLFLTAWTFVTADDSRNGLENLLKTRHEVENPKASRSGGRCRPGGTV
CGFPKPGPYCCSGWCFVCA (SEQ ID NO:399)

Toxin Sequence:

- 10 Cys-Arg-Xaa3-Gly-Gly-Thr-Val-Cys-Gly-Phe-Xaa3-Lys-Xaa3-Gly-Xaa3-Xaa5-Cys-Cys-Ser-
Gly-Xaa4-Cys-Phe-Phe-Val-Cys-Ala-[^] (SEQ ID NO:400)

- 15 **Name:** Sx6.6
Species: striolatus
Isolated: No
Cloned: Yes

- 20 **DNA Sequence:**

ATGAAACTGACGTGCGTGATGATCGTTGCTGTGCTGTTCTTGACTGCCTGGACATTC
GTCACGGCTGATGACTCCAAAAATGGACTGGAGAATCATTTTTGGAAGGCACGTGA
CGAAATGAAGAACCGCGAAGCCTCTAAATTGGACAAAAAGGAAGCCTGCTATCCGC
CTGGTACTTTTTGTGGCATAAAGCCCGGGCTATGCTGCAGTGAGTTGTGTTACCGG
CCGCTCTGCGTCGGTGGTTAACTGCCGTGATGTCTTCTATTCCCCTC (SEQ ID NO:401)

Translation:

- 30 MKLTCVMIVAVLFLTAWTFVTADDSKNGLENHFWKARDEMKNREASKLDKKEACYP
PGTFCGIKPLCCSELCLPAVCVGG (SEQ ID NO:402)

Toxin Sequence:

- 35 Xaa1-Ala-Cys-Xaa5-Xaa3-Xaa3-Gly-Thr-Phe-Cys-Gly-Ile-Lys-Xaa3-Gly-Leu-Cys-Cys-Ser-
Xaa1-Leu-Cys-Leu-Xaa3-Ala-Val-Cys-Val-Gly-# (SEQ ID NO:403)

- 40 **Name:** Sx6.7
Species: striolatus
Isolated: No
Cloned: Yes

- 45 **DNA Sequence:**

ATGAAACTGACGTGTCTGATGGCTGTTGCTGTGCTGTTCTTGACCGCCCGGACATTC

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008237.12800

GTCACGGCTGATGACTCCAGAAATGGATTGGAGAATCTTTCTCCGAAGGCACGTCA
CGAAATGAAGAACCCCGAAGCCTCTAAATCGAACAAGAGATATGAGTGTATTCTA
CTGGTACATTTTGTGGCATCAACGGAGGACTCTGCTCGACGAACCTTTGCTTATTTTT
CGTGTGCTTAACATTTTCGTGATGTCTTCTATCCCTC (SEQ ID NO:404)

Translation:

MKLTCLMAVAVLFLTARTFVTADDSRNGLENLSPKARHEMKNPEASKSNKRYECYST
GTFCGINGGLCCSNLCLFFVCLTFS (SEQ ID NO:405)

Toxin Sequence:

Xaa5-Xaa1-Cys-Xaa5-Ser-Thr-Gly-Thr-Phe-Cys-Gly-Ile-Asn-Gly-Gly-Leu-Cys-Cys-Ser-Asn-
Leu-Cys-Leu-Phe-Phe-Val-Cys-Leu-Thr-Phe-Ser-^ (SEQ ID NO:406)

Name: Sx6.8
Species: striolatus
Isolated: No
Cloned: Yes

DNA Sequence:

ATGAAACTGACGTGTATGGTGATCGTCGCCGTGCTGCTCCTGACGACCTGTCATCTC
ATCACAGCTGATGACTCCAGAGGTACGCAGAAGCATCGTCCCTGAGGTCGACTAC
CAAAGTCTCCAAGTCGACTAGCTGCATGAAAGCCGGGTCTTATTGCGTCGCTACTAC
GAGAATCTGCTGCGGTTATTGCGCTTATTTCGGCAAAATATGTAATTGGCTATCCCAA
AAACTGATCCTCCCCCTACTGTGCTCTATCCTTTCTGCCTGATGTCTTCTCCTCCCC
TC (SEQ ID NO:407)

Translation:

MKLTCMVIVAVLLLTCHLITADDSRGTKHRSRSTTKVSKSTSCMKAGSYCVATTRI
CCGYCAYFGKICIGYPKN (SEQ ID NO:408)

Toxin Sequence:

Ser-Thr-Ser-Cys-Met-Lys-Ala-Gly-Ser-Xaa5-Cys-Val-Ala-Thr-Thr-Arg-Ile-Cys-Cys-Gly-Xaa5-
Cys-Ala-Xaa5-Phe-Gly-Lys-Ile-Cys-Ile-Gly-Xaa5-Xaa3-Lys-Asn-^ (SEQ ID NO:409)

Xaa1 is Glu or γ -carboxy-Glu
Xaa2 is Gln or pyro-Glu
Xaa3 is Pro or hydroxy-Pro
Xaa4 is Trp or bromo-Trp
Xaa5 is Tyr, ¹²⁵I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr

Xaa6 is Nle

^ is free carboxyl or amidated C-terminus, preferably free carboxyl

is free carboxyl or amidated C-terminus, preferably amidated

TABLE 2

Alignment of Conotoxin Peptide Sequences

8-GmVIA [F15Y]	-VKPCRKKEGQLCDPIYQN---CCRGWNC---VLF-CV^ (SEQ ID NO:4)
8-GmVIA [F27Y]	-VKPCRKKEGQLCDPIYQN---CCRGWNC---VLY-CV^ (SEQ ID NO:5)
Omaria9	M---CRREAQLCDPIYQN---CCHGLFC---VLV-CV^ (SEQ ID NO:8)
10 Tx6.11	QVKPCRKKEHQLCDLIFQN---CCRGWYC---VVLSCV^ (SEQ ID NO:11)
Om6.6	---CVPHEGRCNWLTON---CCSGYNC---IIFCL^ (SEQ ID NO:14)
Da6.2	QVKPCRKKEHQLCDLIFQN---CCRGWYC---LLRPECI^ (SEQ ID NO:17)
Da6.6	-VKPCSEEGQLCDPLSQN---CCRGWNC---VLVSCV^ (SEQ ID NO:22)
8-TxVIA [M8J]	W---CKQSGEXCNLLDQN---CCDGY-C---VLVLCV^ (SEQ ID NO:24)
15 Da6.4	---CLGGGEVCDIFFPQ---CC-GY-C---ILLFCT^ (SEQ ID NO:37)
Gm6.5	---CRLGAESCVDISQN---CQQT-C---VFF-CLF^ (SEQ ID NO:40)
Gm6.6	---CKQADESCNVFSLD---CCTGL-C---LGF-CVS^ (SEQ ID NO:43)
Gm6.3	---CVPYEGPCNWLTON---CCDEL-C---VFF-CL^ (SEQ ID NO:46)
20 M6.5	---CKQADEPCDVFSLE---CCTGI-C---LGF-CTW^ (SEQ ID NO:49)
Tx6.2	---CLDAGEVCDIFFPT---CC-GY-C---ILLFCA^ (SEQ ID NO:52)
Om6.1	---CLAEHETCNIFTON---CEGV-C---IFI-CVQAPE^ (SEQ ID NO:57)
Om6.3	---CIPHFDPCDPIRHT---CCFGL-C---LLIACI^ (SEQ ID NO:60)
Om6.4	---CLGFGACILLYSD---CC-GY-C---VGAICL^ (SEQ ID NO:63)
25 Au6.1	---CKAENELCNIFION---CCDGT-C---LLI-CIQNPQ^ (SEQ ID NO:66)
Au6.2	---CLEFGELCNFFFPPT---CC-GY-C---VLLVCL^ (SEQ ID NO:69)
Da6.5	---CAQSSSELCDALDSD---CCSGW-C---MVFFCL^ (SEQ ID NO:72)
Di6.4	---CLGFGACILLYSD---CC-SY-C---VGAICL^ (SEQ ID NO:75)
Pn6.2	---CVKYLDCDMLRHT---CCFGL-C---VLIACI^ (SEQ ID NO:78)
Pn6.3	---CLGFGVPCNFFFPN---CC-SY-C---VALVCL^ (SEQ ID NO:81)
30 Pn6.4	---CIPQFDCDPMVRHT---CCKGL-C---VLIACSKTA^ (SEQ ID NO:84)
Pn6.7	---CKAESEACNIITQN---CCDGT-C---LFF-CIQIPE^ (SEQ ID NO:87)
Omaria3	---CIDGGEICDIFFPN---CCSGW-C---IILVCA^ (SEQ ID NO:90)
Omaria1	---CLDGGEICGILFPS---CCSGW-C---IILVCA^ (SEQ ID NO:93)
Marm7	---CLEFGEVCFNFFPT---CC-GY-C---VLLVCL^ (SEQ ID NO:96)
35 Marm12	---CQEFGEVCFNFFPD---CC-GY-C---VLLVCL^ (SEQ ID NO:99)
Omaria7	---CIPHFDPCDPIRHT---CCFGL-C---LLIACI^ (SEQ ID NO:102)
Omaria11	---CLFGEVPCNFFFPN---CC-GY-C---VLLVCL^ (SEQ ID NO:105)
O6.5	SKQKCRQNGEVCANLH---CCSGP-C---PLF-CLNQBP^ (SEQ ID NO:108)
40 Af6.8	---CTQSGELCDIDFDP---CCNPF-C---IIFCTI^ (SEQ ID NO:111)
KK-2A	---CAPFLHLCITFFFPN---CCNGY-C---VQFICL^ (SEQ ID NO:114)
KKM1	---CLDAGEMCDLFNSK---CCSGW-C---IILFCA^ (SEQ ID NO:117)
KKM4	---CLDGGEICGILFPS---CCSGW-C---IILVCA^ (SEQ ID NO:120)
KKM5	---CENGTGELCDVVEQN---CCYTY-C---FIVVCI^ (SEQ ID NO:123)
45 KKM6	---DDECEPPGDFCGFFKIGP---PCCSGW-C---FLW-CA^ (SEQ ID NO:126)
C. striatus S2	---DDECEPPGDFCGFFKIGP---PCCSGW-C---FLW-CA^ (SEQ ID NO:129)
Om6.5	---DDCEPPGNFCGMKIGP---PCCSGW-C---FFA-CA^ (SEQ ID NO:132)
Au6.3	---DYDCEPPGNFCGMKIGP---PCCSGW-C---FFA-CA^ (SEQ ID NO:135)
Marm9	---DDCEPPGNFCGMKIGP---PCCSGW-C---FFA-CA^ (SEQ ID NO:138)
50 Rg6.4	---D-CLSKNAFCWPIILGP---LCCSGW-C---LYV-CM^ (SEQ ID NO:141)
R6.5	---GDDECLAVKKNCGFPLKGG---PCCSGL-C---FFV-CA^ (SEQ ID NO:144)
Rg6.2	---CLPRDTFCALPQLGL---LCCSGR-C---LLF-CV^ (SEQ ID NO:147)
A6.5	---DG-CSNAGAFCCG---IHPGLCCSEI-C---IVM-CT^ (SEQ ID NO:150)
8-PVIA [F9A]	---EA-CYAOGTACG---IKOGLCCSEF-C---LPGVCFG^ (SEQ ID NO:154)
8-PVIA [I12A]	---EA-CYAOGTFCG---AKOGLCCSEF-C---LPGVCFG^ (SEQ ID NO:155)
55 8-PVIA [T8A]	---EA-CYAOGAFCG---IKOGLCCSEF-C---LPGVCFG^ (SEQ ID NO:156)
M6.3	---DG-CYNAGTFCG---IRPGLCCSEF-C---FLW-CITFVDS# (SEQ ID NO:159)
M6.6	---DE-CYPGTEFCG---IKPGLCCSAI-C---LSCVCSIF-DF^ (SEQ ID NO:162)

M6.7 -EA-CYNAGSFCG---IHPGLCCSEF-C--ILW-CITFVDS# (SEQ ID NO:165)
 M6.8 -EA-CYNAGTFCG---IKPGLCCSAI-C--LSFVCISF-DF^ (SEQ ID NO:168)
 E6.4 -EA-CYPPGTFGC---IKPGLCCSEL-C--LPAPCVG# (SEQ ID NO:171)
 P6.4 -EA-CYPPGTFGC---IKPGLCCSEL-C--LPAPCVG# (SEQ ID NO:174)
 5 δ-SVIE [D1E] -EG-CSSGGTFCG---IHOGLLCCSEF-C--FLW-CITFID^ (SEQ ID NO:177)
 δ-SVIE -DG-CSSGGTFCG---IHOGLLCCSEF-C--FLW-CITFID^ (SEQ ID NO:180)
 C6.2 -YG-CSNAGAFGC---IHPGLCCSEL-C--LVN-CT^ (SEQ ID NO:184)
 C6.3 -YG-CSNAGAFGC---IHPGLCCSEL-C--LGN-CT^ (SEQ ID NO:187)
 Di6.3 -YE-CYLLVHFCG---INGLLCCSNL-C--LFFVCLTFS^ (SEQ ID NO:190)
 10 Rg6.1 -D-CLPDYTICA---FNMGLCCSDK-C--MLV-CLP^ (SEQ ID NO:193)
 Rg6.3 -II-CFPDYMFCG---VNVFLCCSGN-C--LLI-CVP^ (SEQ ID NO:196)
 Gm6.2 ----CYDGGTGCD---SGNQCCSGW-C--IFA-CL^ (SEQ ID NO:199)
 Da6.1 ----CYDGGTGCD---SGNQCCSGW-C--IFV-CL^ (SEQ ID NO:202)
 Pn6.6 ----CFESWVACE---SPKRCCSHV-C--LFV-CT^ (SEQ ID NO:205)
 15 Di6.5 ----CNEAQEHCT----QNDCCSES-CNKFFVGRCLS-D^ (SEQ ID NO:208)
 Af6.10 ----CYDGGTSCN----TGNQCCSGW-C--IFL-CL^ (SEQ ID NO:211)
 T6.10 ----CYDGTSCN----TGNQCCSGW-C--IFVCL^ (SEQ ID NO:214)
 Gm6.4 -D-CQALWDYCPVPLLSGGDCCYGLIC--GPFFVCIW^ (SEQ ID NO:217)
 Om6.2 -K-CQRRWDFCPGSLVGVITCCGLIC--FLFFCV^ (SEQ ID NO:220)
 20 Da6.3 -D-CQEKWDYCPVFPFLGSRYCCDGFIC--PSFFCA^ (SEQ ID NO:223)
 Da6.7 -D-CQGEWEFCIVPVLGFVYCCPWLIC--GPFFVCDI^ (SEQ ID NO:226)
 Pn6.5 -G-CLEVDYFCGIPFVNVNGLCCSGN-C--VFV-C--TPQ# (SEQ ID NO:229)
 Marm6 ----CLNVDFYFCGIPFVNVNGLCCSGN-C--VFV-C--TPQ# (SEQ ID NO:232)
 25 Marm15 -E-CLEADYVCVLFVFGNGMCCSGI-C--VFV-CIAQRKTV^ (SEQ ID NO:235)
 Marm10 -D-CLEPDYVCGIPFVNVNGLCCSGI-C--VFI-CIAQKY^ (SEQ ID NO:238)
 Marm14 -A-CSSKWEYFCIVPVLGFVYCCPLIC--GPFFCV^ (SEQ ID NO:241)
 Omarial4 -D-CLNVDFYFCGIPFVNVNGLCCSGN-C--VF-CLHPTPREVKLP^ (SEQ ID NO:244)
 30 O6.4 ----CLVYGTPCDWLTIAGMECCSKK-C--FMM-CW^ (SEQ ID NO:247)
 R6.4 -D-CHEVGEFCGLPLIKNGLCCSQI-C--LGV-CAKVF^ (SEQ ID NO:250)
 R6.6 -E-CTANGEFCGISVFGSYLCCSGR-C--VFV-CI^ (SEQ ID NO:253)
 R6.7 -E-CTTNGFCGISVFGSYLCCSGR-C--VFV-CI^ (SEQ ID NO:256)
 R6.8 -K-CFPKNHFCGIVFVNLNLYLCCSGR-C--IFV-CV^ (SEQ ID NO:259)
 Rg6.5 -S-CLPLDWFCGFIAGFLCCSGY-C--LVV-CM^ (SEQ ID NO:262)
 35 De6.2 -D-CIPGGENC--DVRFPYRCISGY-C--ILLCA^ (SEQ ID NO:265)
 Striat21 -LRWCIPSGELC--FRSDHIGCCSGK-C--AFV-CL^ (SEQ ID NO:268)
 δStriatus 26 ----WCIPSGDLC--FRSDHIGCCSGK-C--AFV-CL^ (SEQ ID NO:271)
 δStriatus 106 ----WCIPSGDLC--FRSDHIGCCSGK-C--AFV-CL^ (SEQ ID NO:274)
 O6.3 -LRWCVPSPGEC--RRYFVGCSSGK-C--FFV-CS^ (SEQ ID NO:277)
 40 R6.3 ----CLPDGTSC---LFSRIROC-GT-CSSILKCSV^ (SEQ ID NO:280)
 Ak6.1 (F763) ----CRPRGMFCGFPKPGPY-CCNGW-CF--FV-CI^ (SEQ ID NO:328)
 Ar6.11 (G21) ----CLEKGVLCD--PSAGN-CCSGE-CF--LV-CL^ (SEQ ID NO:307)
 Ar6.12 (G20) -E-CVAGSHFCGFPKIGGP-CCSGW-CF--FV-CL^ (SEQ ID NO:310)
 Ar6.5 (F008) -D-CRPVQGYCGIPYKHNRWCCSQL-CA--II-CVS^ (SEQ ID NO:304)
 45 Ca6.5 (G211) ----CVDPGFCG--PGFGD-CCTGF-CL--LV-CI^ (SEQ ID NO:322)
 Ep6.1 (J425) ----CLGFGAEL--MLYSD-CSS-Y-CF-ALV-CL^ (SEQ ID NO:340)
 Ep6.2 (J424) -G-CLEADVYFCGIPFVNVNGLCCSGN-CV--FV-CTPQ# (SEQ ID NO:343)
 G6.3 -DBCEPPGDFCGFFKIGPP-CCSGW-CF--LW-CA^ (SEQ ID NO:283)
 G6.1 (G18) -G-CLDPGYFCGTPPLGAY-CCGGI-CL--IV-CIET^ (SEQ ID NO:337)
 Im6.1 (F076) Q--CRVEGEICGML-FAEQ-CCDGW-CF--FV-CM^ (SEQ ID NO:319)
 50 Lp6.5 (A667) -A-CVELGEICATGFFLDEECCTGS-CH--FV-CVL^ (SEQ ID NO:292)
 Lv6.1 (F775) ----CPNTGELCDV--VEQN-CCYTY-CF-IVV-CL^ (SEQ ID NO:331)
 Mf6.2 (G218) ----CLPENGVLCDL--GSPPYCCSGW-CA-IVV-CI^ (SEQ ID NO:325)
 Mr6.4 (A666) ----CPNTGELCDV--VEQN-CCYTY-CF-IVV-CL^ (SEQ ID NO:295)
 55 Pu6.3 (F770) ----CVEDGDFCG--PGYEE-CCSGF-CL--YV-CI^ (SEQ ID NO:334)
 Qc6.1 ----CAAGAEACVPIIGNVFCCKGY-CL--FV-CIS^ (SEQ ID NO:289)
 Qc6.2 (F024) -DGDGVDGGEFCGFPKIGGP-CCSGW-CF--FV-CL^ (SEQ ID NO:298)
 Qc6.3 (F026) -D-CQDSGVVCGFPKPEPH-CCSGW-CL--FV-CA^ (SEQ ID NO:301)
 Ts6.2 (F078) -D-CWPQYWCFLQRG----CCPGTTFC--FL-CF^ (SEQ ID NO:313)
 60 Ts6.4 (F080) ----WCALDGLCL-IPVIGSIFCCHGI-CM--IY-CV^ (SEQ ID NO:316)
 Tx6.8 ----CYDSGTSC---NTGNQ-CCSGW-CI--FV-CL^ (SEQ ID NO:286)
 Ac6.1 W----CIPRGDLC-FPSDRIQ-CCSGK-CTF---VCM^ (SEQ ID NO:346)

Ac6.2 -G--CVPSGEIC-YFMDHIG-CCSGK-CTF---VCM^ (SEQ ID NO:349)
 Bu6.7 -DE-CSAPGAFCL--IRPGL-CCSEF-C-FF--ACF^ (SEQ ID NO:352)
 Bu6.8 -G--CLPRWEFC-PIFKND-CCSGI-CIS---ICL^ (SEQ ID NO:355)
 Cn6.10 -DG-CYNAGTFCG--IRPGL-CCSEF-C-FL--WCITEVDS# (SEQ ID NO:364)
 Cn6.9 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO:361)
 Cr6.5 W---CIPSGDLC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO:370)
 Cr6.5A ----CIPSGDLC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO:373)
 Cr6.6 ----CIPSGDLC-FPSDHIQ-CCNAK-CAF---VCL^ (SEQ ID NO:367)
 Cr6.6A ----CIPSGDLC-FPSDHIQ-CCNAE-CAF---VCL^ (SEQ ID NO:376)
 Cr6.5B W---CIPSGDLC-FPSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO:379)
 Cr6.6B ----CIPSGDLC-FPSDHIQ-CCNAK-CAF---VCL^ (SEQ ID NO:382)
 Cr6.6C W---CIPSGDLC-FPSDHIQ-CCNAK-CAF---VCL^ (SEQ ID NO:285)
 Cr6.7 W---CIPSGDLC-FPSDHIQ-CCSGK-CTF---VCM^ (SEQ ID NO:388)
 Mn6.3 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO:391)
 Sm6.5 W---CIPSGELC-FRSDHIQ-CCSAK-CAF---VCL^ (SEQ ID NO:394)
 Sm6.6 -DG-CSSGGTFCG--IRPGL-CCSEF-C-FL--WCITFID^ (SEQ ID NO:397)
 Sx6.4 -D--CLAKDAFCAPILGFL-CCSRL-CLY---VCM^ (SEQ ID NO:358)
 Sx6.5 ----CRPGGTVCAGFFKPGPY-CCSGW-CFF--VCA^ (SEQ ID NO:400)
 Sx6.6 -EA-CYPFGTFCG--IKPGL-CCESEL-CLPA--VCVG# (SEQ ID NO:403)
 Sx6.7 -YE-CYSTGTFCG--INGGL-CCSNL-CLFF--VCLTFS^ (SEQ ID NO:406)
 Sx6.8 STS-CMKAGSYCVATTR--I-CC-GY-CAVFGKIGIYPRN^ (SEQ ID NO:409)

X is Nle

It will be appreciated that the methods and compositions of the instant invention can be incorporated in the form of a variety of embodiments, only a few of which are disclosed herein. It will be apparent to the artisan that other embodiments exist and do not depart from the spirit of the invention. Thus, the described embodiments are illustrative and should not be construed as restrictive.

LIST OF REFERENCES

- Barnay, G. et al. (2000). *J. Med. Chem.*
 Bitan, G. et al. (1997). *J. Peptide Res.* **49**:421-426.
 Bodansky et al. (1966). *Chem. Ind.* **38**:1597-98.
 Cartier, G.E. et al. (1996). *J. Biol. Chem.* **271**:7522-7528.
 Cornell-Bell, A.H. et al. (1999). Kainate spiral waves and integrins: A signaling system without gap junctions. *Glia*, in press.
 Craik, D.J. et al. (2001). *Toxicon* **39**:43-60.
 Cruz, L.J. at al. (1976). *Verliger* **18**:302-308.
 Ettinger, L.J. et al. (1978). *Cancer* **41**:1270-1273.
 Fainzilber, M. et al. (1991). *Eur. J. Biochem.* **202**:589-595.
 Fainzilber, M. et al. (1995). *J. Biol. Chem.* **270**:1123-1129.
 Hammerland et al. (1992). *Eur. J. Pharmacol.* **226**:239-244.
 Hillyard, D.R. et al. (1989). *Biochemistry* **28**:358-361.

- Horiki, K. et al. (1978). *Chemistry Letters* 165-68.
- Hubry, V. et al. (1994). *Reactive Polymers* 22:231-241.
- Kapoor (1970). *J. Pharm. Sci.* 59:1-27.
- Kornreich, W.D. et al. (1986). U.S. Patent No. 4,569,967.
- 5 Luer, M.S. & Hatton, J. (1993). *Annals Pharmacotherapy* 27:912-921.
- Martinez, J.S. et al. (1995). *Biochem.* 34:14519-14526.
- McIntosh, J.M. et al. (1982). *Arch. Biochem. Biophys.* 218:329-334.
- McIntosh, J. M. et al. (1998). *Methods Enzymol.* 294:605-624.
- 10 *Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden*, E. Wunsch (Ed.), Georg Thieme Verlag, Stuttgart, Ger. (1974).
- Myers, R.A. et al. (1991). *Biochemistry* 30:9370-9377.
- Nakamura, T. et al. (1996). *Protein Sci.* 5:524-530.
- Nishiuchi, Y. et al. (1993). Synthesis of gamma-carboxylglutamic acid-containing peptides by the Boc strategy. *Int. J. Pept. Protein Res.* 42:533-538.
- 15 Nowak, L. et al. (1984). *Nature* 307:462-465.
- Olivera, B.M. et al. (1984). U.S. Patent 4,447,356.
- Olivera, B.M. et al. (1985). *Science* 230:1338-1343.
- Olivera, B.M. et al. (1990). *Science* 249:257-263.
- Olivera, B.M. et al. (1996). U.S. Patent 5,514,774.
- 20 Ornstein, et al. (1993). *Biorganic Medicinal Chemistry Letters* 3:43-48.
- Plone, M. A. et al. (1996). *Pain* 66:265-70.
- Plummer, J. L. et al. (1991). *J Pharmacol Methods* 26:79-87.
- Rivier, J.R. et al. (1978). *Biopolymers* 17:1927-38.
- Rivier, J.R. et al. (1987). *Biochem.* 26:8508-8512.
- 25 Sambrook, J. et al. (1989). *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.
- Schroder & Lubke (1965). *The Peptides* 1:72-75, Academic Press, NY.
- Shon, K.-J. et al. (1994). *Biochemistry* 33:11420-11425.
- Stewart and Young, *Solid-Phase Peptide Synthesis*, Freeman & Co., San Francisco, CA (1969).
- 30 Suh, H.H. et al. (1992). *Eur J Pharmacol* 213:337-41.
- Vale et al. (1978). U.S. Patent 4,105,603.
- Van de Steen, P. et al. (1998). *Critical Rev. in Biochem. and Mol. Biol.* 33:151-208.
- Woolfe, G. and MacDonald, A. (1944). *J. Pharmacol. Exp. Ther.* 80:300-307.
- Zafaralla, G.C. et al. (1988). *Biochemistry* 27:7102-7105.

09749637.122800

Zhou L.M., et al. (1996). *J. Neurochem.* **66**:620-628.

Zimm, S. et al. (1984). *Cancer Res.* **44**:1698-1701.

U.S. Patent No. 3,972,859.

U.S. Patent No. 3,842,067.

5 U.S. Patent No. 3,862,925.

U.S. Patent No. 5,514,774.

U.S. Patent No. 5,531,001.

U.S. Patent No. 5,534,615.

U.S. Patent No. 5,364,769.

10 U.S. Patent No. 5,545,723.

U.S. Patent No. 5,550,050.

U.S. Patent No. 5,591,821.

U.S. Patent No. 5,719,264.

U.S. Patent No. 5,844,077.

15 PCT Published Application WO 92/19195.

PCT Published Application WO 94/25503.

PCT Published Application WO 95/01203.

PCT Published Application WO 95/05452.

PCT Published Application WO 96/02286.

20 PCT Published Application WO 96/02646.

PCT Published Application WO 96/11698.

PCT Published Application WO 96/40871.

PCT Published Application WO 96/40959.

PCT Published Application WO 97/12635.

25 PCT Published Application WO 98/03189.

PCT Published Application WO 00/23092.

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